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ENDOCRINE STUDIES

XXVI. THE ENDOCRINE INFLUENCE IN STERILITY *

ALLAN WINTER ROWE, PH.D.

BOSTON

In a series of investigations on an objective method for the diagnosis of the diseases of the endocrine glands,[1] the report of a sterile marriage was found to recur with some degree of frequency in the individual case histories. Further, in an appreciable number, it constituted a chief complaint of the patient studied. Still further, in a number of instances in which an existing endocrine condition was demonstrated, its correction by therapeutic measures was followed by productive mating in the couple involved. These observations, by-products of the more extended general investigation, coupled with those deriving from the clinical experience of my colleagues and from studies along other lines, have led to the formulation of a general plan of investigation of the problem of human sterility, preliminary reports of which have already appeared in the literature.[2] The latter investigation includes the study of both partners to an apparently infertile mating, with the evaluation of all the several factors in each to be regarded as causative or contributory. The present report deals with an approach from the opposite point of view and is concerned with the statistical analysis of a long series of patients in whom relative infecundity is correlated with an existing disease condition. That the results from such an approach should lack the clarity of outline of the sterility studies is to be anticipated for several reasons: First, at the time of reference for study the condition elicited may be of recent development and postdate a period of normal productive married life. Second, but one partner of each group is studied, and therefore, as has been clearly shown by the sterility studies, only one half of the potential responsibility can be evaluated.

Although the limitations imposed by these two factors are recognized, it is patent that their effect would be to minimize rather than overemphasize the influences studied. In dealing with consecutive series of patients presenting the conditions under investigation, small percentage differences assume a very real significance, at least in the establishment of a trend.

The patients studied can be divided broadly into three major groups. The first group consisted of persons in whom a definite endocrine condition had been evaluated by a comprehensive diagnostic study,[1] while the second were other patients in the same numerical series in whom the diagnostic investigation had both eliminated an endocrinopathy and demonstrated an existing pathologic condition of nonendocrine etiology. The third group, selected for control, was a consecutive series of 250 healthy women, all pregnant, drawn from a prenatal service.[3] The details of the complete group can be presented most compactly in tabular form, and are collected in table 1.

The nonendocrine group of nearly 900 cases represents a very wide scatter. Approximately one fourth (216) presented infectious processes such as tuberculosis, cholecystitis, severe focal infections and arthritis; ninety-five patients exhibited neuroses, psychoneuroses and psychoses; nearly one fifth (162) demonstrated lesions of the central nervous system, epilepsy, the parkinsonian syndrome, and similar conditions. A group of fifty-six showed various disorders of metabolism; a group of eighty-five showed cardiovascular disorders; seventeen patients had either primary anemia or one of the forms of leukemia; while thirty showed either malignant or benign tumors, the latter including several individuals with nontoxic goiter. One seventh of the group were found to have disorders of the eye, the ear, the skin, the gastrointestinal tract, or to be allergic; fifteen of the women had primary pelvic disorders; fifty-nine of the group were syphilitic; and twenty-seven were normal individuals serving as controls for another investigation.

TABLE 1.—*Group Analysis*

Group	Male	Female	Total
Pituitary	228	479	707
Thyroid	119	262	381
Ovary	0	322	322
Total endocrine	347	1,063	1,410
Nonendocrine	300	589	889
Controls	0	250	250
Grand total	647	1,902	2,549

As has been stated, the group presented was a consecutive series and comprised a number of individuals of both sexes who were unmarried. An analysis of such a group from this standpoint was felt to be possibly significant. In view of the arbitrary character of the figures adopted but basing them on certain rough data from the communities from which these patients were drawn, males less than 26 and females less than 21 years of age were eliminated from further con-

* From the Evans Memorial.

* Read before the Section on Obstetrics, Gynecology and Abdominal Surgery at the Eighty-First Annual Session of the American Medical Association, Detroit, June 27, 1930.

1. Publications from the Evans Memorial: I. Endocrine Studies (1930). A collection of papers which previously appeared serially in Endocrinology, 1928-1930.

2. Meaker, S. R.: The Organization of a Sterility Clinic, J. A. M. A. **91**: 384 (Aug.) 1928. Lawrence, C. H.: J. Maine M. A. **22**: 8 (Jan.) 1929. Meaker, S. R.: Constitutional Factors in the Causation of Sterility, J. A. M. A. **92**: 1493 (May 4) 1929. Meaker, S. R.: New England J. Med. **201**: 160 (July) 1929. Rowe, A. W.: Endokrinologie **7**: 81 (Aug.) 1930.

3. The author is indebted to the staff of the Robinson Memorial for access to these data.

sideration. The data of this portion of the survey are given in table 2.

As will be noted, the endocrine cases designated as "marriageable" show a somewhat wide percentage scatter. The value for the ovarian cases is undoubtedly influenced by the fact that ovarian failure as demonstrated in these investigations occurs only after menstruation has been established. Children in the early part of the second decade, for this reason, are not represented in the ovarian but constitute an appreciable number of the two other endocrine groups. The total percentage of the endocrine group (73) does not differ substantially from that of the group presenting disorders unassociated with the ductless glands. In a like manner the actual percentage of marriage shows a relative agreement, the endocrine group as a whole slightly exceeding the other major section. There is certainly no evidence of a lowered inclination to matrimony in the group presenting endocrine disorders.

TABLE 2.—*Marital Analysis*

Datum	Pituitary	Thyroid	Gonad	Nonendocrine
Total number	707	381	322	889
Unmarried males less than 26 years	111	40	0	113
Unmarried females less than 21 years	114	69	41	95
"Marriageable"				
Number	482	272	281	681
Per cent	68	71	87	76
Married				
Number	290	182	177	406
Per cent	60.2	66.9	63.0	59.6

The age distribution of the married group is collected in table 3.

TABLE 3.—*Age Distribution of Married*

Group	Less Than 21, per Cent	21 to 30, per Cent	31 to 40, per Cent	41 to 50, per Cent
Pituitary	2.4	20.0	44.1	33.5
Thyroid	0	19.8	44.5	35.7
Ovary	1.7	39.5	41.3	17.5
Total endocrine	1.5	25.3	43.5	29.7
Nonendocrine	1.0	20.4	33.5	45.1
Controls	15.6	54.4	26.8	3.2

In the pituitary and thyroid series, nearly four fifths fall between the ages of 31 and 50, correlating well with the nonendocrine group. The ovarian cases show a shift in weight to the earlier decades, and this is even more strikingly shown in the control group. The scatter is significant only as emphasizing the limitations already noted and thus rendering the more significant the ultimate percentage differences in the fecundity.

The duration of married life, as determining the measure of exposure to impregnation, also bears directly on the problem of relative fecundity. These figures are grouped in table 4 for convenience of presentation.

Inspection of the table shows a relative parity between the endocrine and the nonendocrine groups. The average duration for the ovarian cases is the lowest, as might well be anticipated from the preceding table, as the average age of the ovarian cases was less than that of the other series. Broadly speaking, the combined endocrine and nonendocrine fractions show an average duration of about twelve years. The control group, on the other hand, on the average had been married but half of this time. Again recognizing that the value is a purely arbitrary one, I have taken three years as the time in which at least one pregnancy may be reasonably assumed to occur in the average, normal, fecund marriage. It should be said in passing that every effort has been made to secure specific information in every case in regard to contraception, and in the later summaries due allowance has been made for this factor. Broadly speaking, only one tenth of the patients in the endocrine and nonendocrine series were married less than three years, while half of the fertile control group gave a duration within that interval.

In the marriage that fails to produce viable children, three major factors, exclusive of contraception, may be regarded to operate. First, there is the failure to conceive; second, the failure to carry through a successful pregnancy, and, third, the interruption of pregnancy by an induced abortion. This third element is, of course, a purely artificial intervention and therefore devoid of meaning in the estimation of a relative fecundity. An analysis of the number of conceptions

TABLE 4.—*Duration of Married Life*

Group	Total Married	Average Duration, Years	More Than 3 Years, per Cent
Pituitary	290	12.4	91.2
Thyroid	182	11.5	92.3
Ovary	177	9.7	86.4
Total endocrine	649	11.4	89.5
Nonendocrine	406	13.1	91.6
Control	250	6.0	49.6

in the several groups and the distribution of their outcome is significant (table 5).

Study of table 5 exhibits certain rather definite trends. In the first place the pituitary and nonendocrine groups show substantially the same figures for the percentage of conceptions yielding viable children; the thyroid value is a little lower; that for the ovary significantly so. Naturally the total endocrine figure falls somewhat below that of the nonendocrine group in which it may be remembered there were fifty-nine syphilitic patients and an appreciable additional number presenting disease conditions known to influence pregnancy adversely. In the control group the current pregnancies have been omitted, as the outcome was naturally problematic. Dealing solely with those which have been consummated, the productivity of this group is demonstrably at least 10 per cent higher than that of the two other major groups.

TABLE 5.—*Analysis of Conceptions*

Group	Number of Conceptions			Children, per Cent	M scarriages, per Cent
	Gross	Abortions	Net		
Pituitary	602	33	569	80.7	19.3
Thyroid	330	11	319	77.1	22.9
Ovary	304	24	280	71.4	28.6
Total endocrine	1,236	68	1,168	77.5	22.5
Nonendocrine	936	55	881	80.6	19.4
Control	550*	1	549*	87.1	12.9

* Omitting current pregnancies (250), the results of which are not yet known.

Approaching the question from a somewhat different angle, if the total number married in each division is correlated with the actual number of conceptions, it will be found that the control group leads with an average of 3.40 conceptions (including current pregnancies) for each mating. The pituitary value of 2.94 is but slightly less than this; the thyroid figure of 2.58 shows a significant decrement; the ovarian cases with 2.49 are still lower; while the nonendocrine group has

the lowest value of all; namely, an average of 2.31 conceptions for each married pair.

All of the figures given demonstrate a trend but fall far short of indicating the real degree of infertility. The data that they contain, however, are susceptible of further analysis, the end-result of which may be regarded as indicating a tendency, even though the absolute magnitude of the figures lacks the authority intrinsic in larger groups similarly analyzed. These data are given in table 6.

It will be noted that those who have been married less than three years and have failed to conceive have been deducted from the infertile matings. As was stated previously, the figure taken is an arbitrary one but, in my opinion, represents a fair allowance for this element of uncertainty. It should also be noted that the factor of contraception has been eliminated from the figures as presented for the infertile group. A brief review of the table shows a definite infertility of nearly 30 per cent in the pituitary group, slightly more than 30 per cent in the thyroid, and over 35 per cent in the ovarian group. All of these figures exceed, and exceed significantly, the infertility exhibited by the nonendocrine series (20 per cent), though the latter group shows a lowered fecundity which is substantially twice that of the usually accepted figure based on community surveys. Reynolds and Macomber [4] conclude

TABLE 6.—*Analysis of Infertility*

Datum		Pituitary	Thyroid	Ovary	Nonendocrine
Married, number	(a)	290	182	177	406
Conceived, number	(b)	205	128	122	324
Not conceived, number	(c)	85	54	55	82
Not conceived and married less than 3 yrs.	(d)	23	8	20	23
Infertile:					
1. Nonconception (c — d)	(e)	62	46	35	59
2. Miscarriage	(f)	14	8	19	18
3. Abortion	(g)	3	1	4	5
Total infertile (e + f + g)	(h)	102	63	78	105
Net infertile (e + f)	(i)	76	54	54	77
Infertile, per cent (i / a — d — g)	(j)	28.8	31.2	35.3	20.4

that from 10 to 12 per cent represents a fair measure of infertility, and that without allowance for the artificial element of contraception which today must be recognized as a very definite factor. Since it has been carefully excluded from the present survey, it seems fair to assume that the data as presented show not only a lowered fertility through the agency of disease, as might well have been anticipated, but that those patients presenting evidence of an endocrine disorder demonstrate an even greater lowering of fecundity, least marked in the pituitary, and most in the ovarian cases.

SUMMARY AND CONCLUSION

1. A series of sterile marriages has been reported with regard to the coexistence of various diseases. The marriage histories of a group of normal, healthy, pregnant women have served as controls.

2. It appears that endocrine disorders do not result in a decreased number of marriages.

3. The percentage of sterile marriages is highest in those showing ovarian disease, next highest in thyroid, and lowest in pituitary disorders. In the nonendocrine group studied, infertility was definitely less frequent than among those having endocrine disease. Even with the nonendocrine group the incidence of infertility is double that usually regarded as normal for the community.

80 East Concord Street.

4. Reynolds, Edward; and Macomber, Donald: Fertility and Sterility in Human Marriages, Philadelphia, W. B. Saunders Company, 1924.

FUNCTIONAL DISORDERS OF MENSTRUATION

WITH REMARKS ON ORGANOTHERAPY *

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BALTIMORE

Abnormalities in the quantity and rhythm of the menstrual flow are, of course, frequently associated with definite anatomic lesions in the pelvis. This is especially true of menstrual excess, which is much more often due to local than to general causes. The opposite is true of deficiency or absence of the flow, although even complete and permanent amenorrhea may be caused by pelvic disease, as, for example, by lesions which destroy all ovarian tissue.

Even when definite lesions are present, there is little doubt that the associated menstrual abnormalities are often to be explained by disturbances of function rather than by any mechanical effect of the lesions themselves. It is hard, in many instances, to draw the line between the rôles played by pathologic anatomy and pathologic physiology, especially in the present incomplete stage of our knowledge.

In a large group of cases of amenorrhea and scanty menstruation (hypomenorrhea), and also in a considerable proportion of cases of menorrhagia (hypermenorrhea), however, there is no demonstrable lesion of the generative organs, so that it is customary to speak of such cases as of the functional type. Certainly, at any rate, the functional factor is manifested in purest form in this group, and can be studied without the necessity of evaluating the influence of an associated anatomic lesion. Besides the quantitative disorders already mentioned, functional derangement of the sex cycle may manifest itself through disturbances of the menstrual tempo, i. e., too frequent or too infrequent menstruation (polymenorrhea or oligomenorrhea).

OVARIAN THERAPY IN LIGHT OF NEWER KNOWLEDGE OF MENSTRUATION

It is unnecessary to urge that study of the abnormalties of the menstrual cycle must be based on a knowledge of the physiology of normal menstruation. This at once faces us as gynecologists with our problem, for our knowledge of the normal cyclic physiology is still far from complete. From time to time new discoveries make us feel that we are beginning to stand on solid ground, but, in every case the new light has only served to give us a glimpse of still unraveled mysteries. For example, with the discovery, at the very end of the preceding century, of the essential rôle of the ovarian hormone or hormones in the production of menstruation, the problem seemed solved. Our immediate predecessors, in their innocence, at once felt able to distinguish conditions of ovarian excess and, especially, of ovarian deficiency. Spurred on by the then fresh triumphs of thyroid therapy, they were quick to apply the same principles to the new problem. If amenorrhea is the result of absent or deficient ovarian secretion, the mere feeding of ovarian substance was the rational procedure for its relief. And thus, on evidence which now seems pathetically flimsy, sprang

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* Owing to lack of space, this article has been abbreviated in THE JOURNAL. The complete article appears in the Transactions of the Section and in the author's reprints.

up the weedy growth of ovarian therapy which we are now trying to clear away, lest it choke the few hardy plants of truth that have raised their heads since then.

The whole subject of the physiology of the menstrual cycle is still in a very fluid state, and constant readjustment of our concepts will no doubt be necessary for many years to come. Recently (in the Gilliam Memorial Lecture of 1929), I [1] reviewed certain important recent additions to our knowledge which make it necessary to revamp our ideas of the mechanism of menstruation and to discard certain long cherished beliefs. For example, evidence has been brought forward which must make us at least question seriously the indispensability of ovulation to menstruation. Again, the almost universally accepted opinion that the life of the germ cell itself is the dominating influence in the cycle, and the one that determines its periodicity—the doctrine of the "primacy of the ovum"—must be abandoned altogether, with, unfortunately, no satisfactory substitute as yet to take its place. The bearing of this one point alone on the question of the causation of the disorders of menstrual rhythm is obvious, as will be discussed later.

Of more general interest, perhaps, because of the propensity to treat disease with "extracts" of one sort or another, if given any encouragement whatever, are the recent discoveries as to the number, nature and relation of the ovarian hormones. In spite of the demonstration by Fraenkel,[2] in 1903, of the physiologic importance of the corpus luteum, there had been no wholly satisfactory demonstration of the assumed properties of this secretion until about one year ago. Praiseworthy efforts had been made along this line by Papanicolaou,[3] Hisaw,[4] and others, but it was only the recent work of Corner and Allen [5] that demonstrated conclusively the correctness of the views held by many that the corpus luteum produces a principle just as important in the menstrual cycle as the follicle hormone.

Following the demonstration of the potency of the follicle hormone in producing typical estrous effects in the lower animals, there had occurred the usual enthusiastic surge to apply this fact therapeutically, just as soon as commercial preparations of the product became available. I do not believe that any one will maintain that these hopes have been realized, or, indeed, that thus far any worth while therapeutic results have been achieved. There are a number of reasons for this failure, but one of them is the fact that the follicle activity is responsible for only a fraction of the cyclic physiology.

The demonstration of the corpus luteum principle, while of great importance from a physiologic standpoint, does not by any means supply all the scientific groundwork necessary for intelligent organotherapy. For example, nothing can be more certain than that other endocrine glands, especially the pituitary, thyroid and suprarenal, play an important part in sex physiology. One can well believe that the ovary is only the immediate portal of entry through which the entire endocrine chain, functioning almost as if it were a single though composite organ, empties its influence into the female sex apparatus.

With regard to the anterior pituitary lobe, the mechanism of this relation has been brilliantly illuminated by the studies of Smith and Engle,[6] and Evans and Long [7] in this country, and of Zondek and Aschheim [8] in Germany. The extremely powerful effects produced on the ovary, and through it on the generative canal, by repeated implantations of anterior pituitary tissue, demonstrate beyond question the importance of the latter in the physiology of the cycle, and—the point with which we are concerned in the present discussion—with its probable importance in many menstrual disorders that in the past were looked on as purely pelvic problems, so to speak. As a basis for later discussion, it is important to remember that the hypophyseal hormone has no direct effect on the genital mucosa, but exerts its effect on the ovaries, so that it has been designated as the "motor of the ovaries." In this lies the chief difference as compared with the follicle substance, which produces a direct estrous effect on the genital mucous membranes, even in animals which have been previously castrated. For a fuller discussion of these physiologic problems I would refer to my previous paper.[1]

There is still much to learn as to the part played in menstruation and its disorders by such organs as the thyroid and suprarenal. Riddle,[9] with much justification, states that "nearly all of the internal secretions are intimately concerned in one or other special aspect of reproduction." He has demonstrated definite seasonal variations in the size of a number of the ductless glands, apparently related to periods of active or inactive reproduction. He believes that the essential processes of reproduction are not under the control of the nervous system. This, however, is not equivalent to saying that the cycle cannot be affected through the nervous system. In the human being, for example, there is ample evidence that nervous and psychic factors may occasionally be important in the production of disorders of menstruation.

Even our present incomplete knowledge indicates a far greater intricacy of the cyclic mechanism than had been anticipated. The reproductive function, because of its essential importance in the perpetuation of the species, seems to be physiologically more deeply rooted than almost any other. This very intricacy of mechanism makes the interpretation of menstrual disorders correspondingly difficult. My discussion of these disorders, therefore, will be disappointingly lacking in sharpness and definition, because of the poor light afforded by our present knowledge. It will deal with broad principles rather than with rules of thumb.

FUNCTIONAL AMENORRHEA AND HYPOMENORRHEA

Functional amenorrhea and functional hypomenorrhea may be discussed together because, so far as is known, the underlying causes are the same. They constitute the largest and most important type of amenorrhea and hypomenorrhea, for local causes, other than the physiologic ones, are relatively uncommon and usually not difficult to recognize. The causes of functional amenorrhea may be grouped into the constitutional and the endocrinopathic, although it is not always easy to draw the line between them.

Constitutional.—It has long been known that constitutional diseases of various sorts, associated as they

1. Novak, Emil: Recent Advances in the Physiology of Menstruation, J. A. M. A. **94**: 833 (March 22) 1930.
2. Fraenkel, L.: Arch. f. Gynäk. **68**: 438, 1903.
3. Papanicolaou, G. N.: A Specific Inhibitory Hormone of the Corpus Luteum, J. A. M. A. **86**: 1422 (May 8) 1926.
4. Hisaw, F. L.: Physiol. Zool. **2**: 59 (Jan.) 1929; J. Exper. Zool. **42**: 411, 1925.
5. Corner, G. W., and Allen, W. M.: Am. J. Physiol. **88**: 326 (March) 1929.
6. Smith, P. E., and Engle, E. T.: Am. J. Anat. **40**: 159 (Nov.) 1927.
7. Evans, H. M., and Long, J. A.: Anat. Rec. **21**: 62, 1921.
8. Zondek, Bernhard, and Aschheim, S.: Arch. f. Gynäk. **130**: 1 (April) 1927.
9. Riddle, Oscar: Endocrinology **13**: 311 (July-Aug.) 1929.

are with deterioration of the general health, are often characterized by deficiency or absence of menstruation. The latter, therefore, are frequently symptoms of tuberculosis, chronic nephritis, diabetes, and similar debilitating diseases. Amenorrhea is not infrequently found in even incipient tuberculosis, and it may, indeed, be the first symptom noted by the patient.

The various forms of anemia are even more important in this regard. None of the older textbooks failed to elaborate on the frequency and importance of chlorosis in this regard, though now it appears to be a vanishing disease. The explanation of amenorrhea produced by these debilitating diseases has in the past been that it represents an effort on the part of nature to conserve the strength of the patient. Nothing, however, could be said of the mechanism. The experimental studies of McCollum [10] and others, however, have demonstrated that the ovary is singularly sensitive to nutritional influences. This is most clearly seen in the effects produced by deficiencies in the vitamin content of the diet, for dietary defects of this type quickly produce in animals a disappearance of the sex cycle. That the same effect is produced in the human female was illustrated on a grand scale in the "Kriegsamenorrhöe" so widely prevalent throughout the belligerent countries during the privation days of the World War. The immediate ovarian effect produced by this cause is probably an interference with the maturation of the follicles, and, of course, with ovulation.

The present-day prevalence of self-dieting, often extreme, among women makes this cause of amenorrhea of anything but academic interest. While the diet of the average American woman contains a sufficient proportion of the essential vitamins, exceptions are at times found, and are common in the case of women making strenuous efforts to reduce.

Little need be said as to the treatment of amenorrhea due to the causes enumerated here, for it is obviously to be directed to the cause of the disorder. For example, the rational procedure in cases of tuberculosis or anemia is the treatment of these conditions, just as, in the management of amenorrhea due to dietary errors, insistence on a properly balanced diet will effect a cure. Perhaps the most important injunction is to abstain from any direct treatment of the menstrual disorder, whether by the old-fashioned emmenagogue drugs or by the more modern organ extracts. Such measures are irrational, often harmful, and almost always unsuccessful.

Endocrinopathic Amenorrhea and Hypomenorrhea.—This is perhaps the most frequent and most interesting of all types. Its mechanism is varied, and on this variation are based certain clinical syndromes presented by the patients, placing them under different categories. For example, it is customary to speak of a *hypogonadal* and a *hypopituitary* type, while *thyroid* hyperfunction, and, less commonly, thyroid hypofunction, may likewise be of causal importance. It should be recognized, however, that these terms are not based on any exact knowledge of the nature of the relationship implied.

In the so-called hypogonadal type, the endocrine effect is believed to involve chiefly and perhaps only the ovary. The prototype of this variety is the normal amenorrhea after the menopause, or, though not so physiologic, that seen after complete removal of ovarian tissue. One would expect, therefore, to find the subjective and objective conditions similar to those seen after the menopause, but there are numerous exceptions to this. From a subjective standpoint it is true that vasomotor symptoms may be noted, though they are rarely troublesome. There may be moderate or at times marked adiposity, with the heaviest deposits about the abdomen and hips. In other cases, however, where no other endocrine factor than the ovary can be demonstrated, and where other constitutional factors likewise are lacking, there may be no gain, and perhaps even some loss of weight. In short, the tendency has been to apply the designation of "hypogonadal" to cases in which these other factors cannot be established. The precariousness of such a deduction is obvious.

The endocrinopathic cause of amenorrhea for which the most satisfactory scientific evidence is available is that due to anterior pituitary deficiency. This type of amenorrhea is associated with adiposity, sometimes moderate, at other times quite marked. In one of my patients, there had been a gain of 90 pounds, (41 Kg.) in one year. The deposit of adipose tissue shows a rather characteristic distribution, with often large shoulder pads, rather large bust, a narrow waist, and heavy deposits about the abdomen, buttocks and hips. The hands are small and delicate, and the fingers slender and rather pointed. There may be little in the way of subjective symptoms, though headache ("pituitary headache") is sometimes complained of. This clinical picture has been rather firmly established in the literature as adiposogenital dystrophy, or Fröhlich's syndrome. It was originally described by Fröhlich [11] in association with a pituitary tumor but is now accepted as occurring with purely functional pituitary deficiency.

There is a sound experimental basis for this view in the studies of Cushing and his co-workers,[12] who demonstrated that partial ablation of the anterior pituitary in female dogs is followed by obesity, together with hypoplasia of the generative organs, manifested clinically by a disappearance of the sex cycle. There has been much discussion as to whether all these symptoms are really of pituitary origin, but the recent studies of Smith [13] appear to leave no doubt that the adiposity is due to associated disturbance of the adjoining hypothalamus, while the changes in the genital tract are unquestionably of anterior pituitary origin. The fact remains, however, that there is a characteristic clinical association between the two sets of changes, so that the resulting syndrome is still commonly designated as adiposogenital dystrophy.

Functional disturbance of the thyroid may likewise be characteristized by amenorrhea or hypomenorrhea as one of the symptoms. This is more frequently the case with hyperfunction than with hypofunction, which, in my experience, is more commonly characterized by menstrual excess. There are, however, numerous exceptions to both these statements, thus confusing the exact nature of the thyroid influence on the menstruation. As with amenorrhea of the hypopituitary type, there is commonly a tendency to obesity if the thyroid function is deficient. The adipose tissue, however, is more evenly distributed, with little tendency to the localizations described in connection with the pituitary variety, and it may show some degree of the infiltrative myxedematous thickening seen so often with hypothyroidism.

If, as is perhaps more often the case, the amenorrhea is associated with hyperthyroidism, the well known

10. McCollum, E. V.: The Newer Knowledge of Nutrition, ed. 2, New York, Macmillan Company, 1922.

11. Fröhlich, Alfred: Wien. klin. Rundschau **15**: 883, 1901.
12. Cushing, Harvey; Crowe, S. J., and Homans, J.: Bull. Johns Hopkins Hosp. **21**: 127, 1910.
13. Smith, P. E.: Am. J. Anat. **45**: 205 (March 15) 1930.

characteristics of the latter condition are seen to greater or less degree. I need not stress the importance of studies of basal metabolism in the proper evaluation of these cases, or in their proper management. For that matter, they can rarely be dispensed with in the proper interpretation of any endocrinopathic menstrual disorder.

Associated Symptomatology of Endocrinopathic Amenorrhea.—In a large proportion of cases, there has been, in my experience, little or nothing in the way of subjective symptoms. At times, especially in the hypogonadal cases, there has been a complaint of vasomotor flushes, but these have only occasionally been very troublesome. The same thing may be said of the vertigo occasionally observed. Headache is not infrequent in cases of the adiposogenital dystrophy group.

Nervousness and depression are rather common, but I believe they are due in large measure to the psychic effect produced by the absence of menstruation. This, in turn, is often due to the wrong ideas held by many of the laity as to the significance of menstruation. The belief is still prevalent among the laity that the purpose of the menstrual flow is the purgation of the woman's system of impurities, and that abolition of the function causes a retention of these harmful substances. Again, a superstition often encountered, especially among the less intelligent, is that amenorrhea may lead to consumption, that the girl who does not menstruate is likely to "go into decline." This belief no doubt has its origin in the fact that in many cases of actual tuberculosis amenorrhea is an associated symptom.

In the case of married women who are anxious for pregnancy, the sterility which so often accompanies long standing amenorrhea introduces another factor of the greatest importance in producing nervous and psychic symptoms. In general there is no doubt that amenorrhea greatly lessens the woman's chances for pregnancy, although exceptions are not infrequently observed. I have seen pregnancy supervene in a number of cases in which the women had not menstruated for several years. Taken as a whole, it is this group of cases of amenorrhea, i. e., those in which sterility is the underlying complaint, that most often calls for efforts at correction. Among women in whom the picture of the amenorrhea is not confused and overshadowed by the desire for children, it is in a large proportion characterized by few or no symptoms, and the patient may be in as good health as if she menstruated regularly. This statement does not, of course, apply to the far less frequent cases in which some organic lesion, such as a pituitary tumor, is present.

Diagnosis.—From what has been said, it is evident that amenorrhea is merely a symptom of some underlying condition, and not an entity in itself, to be treated by this or that form of organic extract. Every effort must be made to classify the individual case on the basis of careful history and physical examination, with such aids as the laboratory can offer. The latter will often mean such measures as roentgenologic study of the sella turcica, urinalysis, tests of sugar tolerance and studies of basal metabolism. The more obvious types due to such definite diseases as tuberculosis and anemia are determinable by the usual diagnostic methods. The history should be complete enough to bring out such factors as dietary defects, changes in weight, and endocrinopathic manifestations such as marked fluctuations of weight. The physical examination will, of course, include such details, important in endocrinopathic study, as the presence or absence of obesity, the distribution of the adipose tissue, the distribution of hair, the height of the patient, and the condition of the pelvic organs.

Treatment.—There are a good many cases in which endocrinopathic amenorrhea needs no treatment, others in which the treatment need be only a reassurance as to the essential harmlessness of the condition in itself, and still others in which efforts at correction are definitely indicated. To the first group belong the cases of moderate severity, with no subjective symptoms, in which pregnancy is not an important consideration. For example, a woman aged perhaps 35 to 37, whether married or unmarried, will usually choose to forego any treatment if convinced of the harmlessness of the disorder and the usual unsatisfactoriness of the treatment. She will be quite willing to resign herself to a premature menopause, which is about what the condition represents.

In women who have been much perturbed and depressed by the amenorrhea, and especially when this upset is due to such erroneous ideas as I have mentioned previously, the physician can perform a real service by explaining in simple language the real significance of menstruation, stressing the fact that complete absence of the periods is compatible with good health. In a considerable number, however, it is advisable to resort to treatment, with a frank explanation to the patient as to its limitations.

The third group presents the clearest indication for treatment. It includes those cases in which there are definite associated symptoms, and, more particularly, when an associated sterility, otherwise unexplainable, constitutes the problem of immediate concern to the patient. Aside from measures of general hygiene and procedures directed to the improvement of general health, organotherapy of one form or another is the first thought of most practitioners in the treatment of most cases of this group. If based on rational indications, this is, of course, fully justified; but it should be remembered that the organotherapy of endocrinopathic amenorrhea is rather unsatisfactory and with great frequency unsuccessful. I have elsewhere fully reviewed the entire subject of ovarian therapy.[14] Regardless of the possible value of the oral administration of certain ovarian preparations for the subjective symptoms of menstrual deficiency, though even this is open to some question, a review of the literature and a rather large personal experience have convinced me that they have no value in the reestablishment of menstruation in cases of amenorrhea. It is of interest to note that the Council on Pharmacy and Chemistry, after an impartial review of the question, has just decreed the omission of all such preparations from New and Nonofficial Remedies. The same pessimistic statement may be made of the various preparations introduced for hypodermic administration, up to the discovery of the potency of follicle hormone in producing the sex cycle in laboratory animals that had been previously castrated.

As I stated earlier in this paper, the results of follicle hormone therapy in amenorrhea have thus far been extremely disappointing. Its chief value, thus far, has been in the diagnostic field, in the hands of the small group of investigators who have utilized it in this way. Studies of the follicle hormone content of the blood have apparently been of help in differentiating conditions of excess and deficiency, although even this aspect of the work has scarcely passed out of the experimental phase. The problem is further confused by the fact

14. Novak, Emil: The Present Status of Ovarian Therapy, J. A. M. A. **91:** 607 (Sept. 1) 1928.

that even amenorrhea may be associated with an excess rather than a deficiency of follicle hormone in the blood (polyhormonal amenorrhea), as shown by Zondek [15] and others. A number of reports have been made as to the production of menstruation by injections of follicle hormone, but they are few and unimpressive. Even when uterine bleeding is produced, it is almost certainly not a genuine menstruation, for the follicle hormone cannot itself complete the menstrual cycle. It probably can bring about a certain degree of hyperemia and hypertrophy of the endometrium, even in human females, if given in sufficiently large dosage, and this may at times be followed by bleeding. But this is not menstruation, for among other things, the ovary plays no part in it, and the endometrial changes are quite different.

The effect of the follicle hormone is exerted on the genital mucosa alone, so that it is to be looked on as purely substitutional and transient. There is no tendency toward a reestablishment of the ovarian cycle, so that it would be necessary to repeat the injections whenever the patient wished to menstruate. There are few patients so anxious to menstruate that they would be willing to continue indefinitely with such treatment, especially when it involves many disagreeable hypodermic injections for every course of treatment. Furthermore, there is not the slightest reason to expect that it would enhance the patient's chances for pregnancy. This question of follicle hormone therapy is fully discussed in a previous paper.[16]

Since the writing of that paper, two other methods of administering ovarian follicle substance have been suggested to obviate the necessity of repeated hypodermic injections. One is the method of administration by vaginal suppository, with which I have had only a limited experience. The other plan, recently suggested by Pratt and Smeltzer,[17] is that of the nasal spray, as the hormone apparently enters the circulation of the patient when given in this way. Neither method can hope, however, to bring about any more potent results than the method of direct hypodermic injection. Since the latter itself is admittedly unsatisfactory in its results, there is little reason to expect any wide adoption of these newer methods, in spite of their lessening of the patient's discomfort.

Within the past few months, Doisy, Veler and Thayer [18] in this country, and Butenandt [19] in Germany, have announced the isolation of this hormone in crystallized form. These crystals are of enormous potency, Doisy and his co-workers stating that each grain of their substance possesses the potency of two million rat units. A substance as powerful as this may some day prove to be of great value therapeutically, but the foregoing pessimistic remarks are based on conditions as they now are, and I believe that they are justified.

In previous papers I have emphasized the fact that the endometrial preparation for menstruation is really a preparation for a possible pregnancy, and that the corpus luteum is just as important in the cycle as is the follicle. If, therefore, an active corpus luteum principle could be isolated, there would be reason to believe that the normal sequence of events in human menstruation could be mimicked much more completely than with follicle hormone alone.

An active corpus luteum extract has recently been prepared by Corner and Allen,[5] although it is not yet available commercially. It will be interesting to see whether the sequence of injections of follicle hormone, followed by injections of corpus luteum hormone, according to the plan which I suggested in 1922, will bring about menstruation more often than injections of follicle hormone alone. This principle, which I have repeatedly urged on the basis of what has been known as to the histologic interrelationships of menstruation, has been firmly established by the work of Willard Allen [20] and of Hisaw.[21] Both of these investigators have demonstrated that the corpus luteum hormone can bring about the characteristic pregravid changes in the endometrium only when the latter has been adequately prepared for this by injections of the follicle hormone. Even the combined plan of treatment, however, would be a substitutional rather than a permanently stimulating treatment, so here again it will probably not have a wide appeal in the treatment of amenorrhea.

Far more promising appears to be the field opened up by recent work demonstrating the effect on the ovary of the anterior pituitary hormone. The method of implantation, used for experimental work, would not be practicable clinically, but already efforts at obtaining the active principle in a form suitable for clinical use are being made.

The oral administration of pituitary substance, on the basis of laboratory studies, is probably worthless, although I am well aware that it is employed by many excellent clinicians, especially in the treatment of adiposogenital dystrophy. My own impression has been, however, that any benefit which commercial preparations of anterior pituitary substance have seemed to confer has come from the thyroid extract which has almost always been combined with them. Within the past few months Collip [22] has published studies which indicate that the oral administration of properly prepared extracts are potent in doses only two or three times as great as those required for hypodermic administration. These results contradict those of Smith and Engle, and other investigators, so that the status of the question is still unsettled. In a very small group of cases of ovarian hypofunction which Campbell and Collip [23] treated by the oral administration of their extract, encouraging results were obtained, but these observations obviously call for multiplication and confirmation. Zondek,[24] Biedl,[25] Seitz [26] and others have likewise been experimenting with anterior pituitary therapy, though by the hypodermic route. Little has as yet been achieved, and the method is said not to be devoid of risk. In spite of its great promise, therefore, this plan of therapy is as yet undeveloped and, of course, inaccessible to most clinicians.

As a matter of fact, thyroid extract still remains the sheet anchor in the treatment of functional amenorrhea, as in so many other endocrinopathies. Its rationale is not always clear, except, of course, when a definite hypothyroidism is present. Even in the absence of the latter, however, the thyroid substance is commonly employed on empiric or semiempiric grounds. It will

15. Zondek, Bernhard: Zentralbl. f. Gynäk. **54:** 1 (Jan. 4) 1930.
16. Novak, Emil: Endocrinology **11:** 173 (May-June) 1927.
17. Pratt, J. P., and Smeltzer, Merrill: Endocrinology **13:** 321 (July-Aug.) 1929.
18. Doisy, E. A.; Veler, C. D., and Thayer, S.: Am. J. Physiol. **90:** 329 (Oct.) 1929.
19. Butenandt: Die Naturwissenschaften **17:** 879, 1929.
20. Allen, W. M.: Am. J. Physiol. **92:** 612 (April) 1930.
21. Hisaw, F. L., and Leonard, S. L.: Am. J. Physiol. **92:** 574 (April) 1930.
22. Collip, J. B.: Canad. M. A. J. **22:** 215 (Feb.) 1930.
23. Campbell, A. D., and Collip, J. B.: Canad. M. A. J. **22:** 219 (Feb.) 1930.
24. Zondek, Bernhard: Klin. Wchnschr. **8:** 157 (Jan. 22) 1929.
25. Biedl, A.: Endokrinologie **2:** 241 (April) 1929.
26. Seitz, Ludwig: Monatschr. f. Geburtsh. u. Gynäk. **84:** 79 (Feb.) 1930.

usually reduce the weight and may cause some subjective improvement, but it will only occasionally restore menstruation, except in the cases of outspoken hypothyroidism.

All in all, therefore, the endocrine treatment of amenorrhea must still be viewed pessimistically, in spite of the glowing promises of successful results pictured in the literature of many manufacturers of organ extracts. Of other methods of treatment, such as radiotherapy of the ovaries and pituitary body, I can say little from personal experience. They have been employed by a number of gynecologists, but the methods do not seem to have achieved any great vogue, which does not argue for any brilliance of result. Rubin,[27] Rongy,[28] and others have reported good results from light roentgenization of the ovaries, but I agree with Frank that the method should be used with great caution, for fear of destroying the follicle apparatus in an already deficient ovary.

FUNCTIONAL MENORRHAGIA (HYPERMENORRHEA)

The subject of functional menorrhagia I shall discuss in only a summarizing fashion, as I have elaborated on it in a number of previous papers.[34] It is seen only during the reproductive epoch and occurs most characteristically at or near the menopause and, less frequently, at or shortly after puberty. It may, however, occur at any period of menstrual life. As a rule the pelvic organs show no demonstrable lesion. The characteristic ovarian finding is an absence of corpora lutea and the presence of a persistent graafian follicle. The endometrium usually shows a characteristic picture, designated as hyperplasia of the endometrium. This, however, is merely the result of the ovarian disturbance, which evidently consists in a persistence of the follicle effect, with no secretory or desquamative changes in the endometrium.

It has been generally believed that the immediate ovarian disturbance associated with functional bleeding consists of an excess or persistence of the follicle stimulus, while the corpus luteum activity is in abeyance. Recent studies,[24] however, indicate that in some cases of amenorrhea a similar excess of the follicle principle is found in the blood, and that the endometrium may in such cases even exhibit a definite hyperplasia. I have myself seen typical hyperplasia of the endometrium in an amenorrheic woman, so that this endometrial lesion cannot be considered to be as constantly associated with abnormal bleeding as has been heretofore believed.

The type of menorrhagia under discussion, however, is certainly of functional origin. Whether the disturbance is really primarily in the ovary or whether it originates elsewhere in the endocrine chain, it is difficult to say. Certainly there are cases of menorrhagia of thyroid origin, as already mentioned, but these are far less frequent than the type under discussion, which can be considered one of the common menstrual disorders.

For the treatment of this disorder, as well as for a full discussion of its clinical and pathologic characteristics, I would refer to my previous papers on the subject.[34] Two new aspects of the problem, however, may be indicated.

The first is the possibility that the anterior pituitary may play an important part in the causation of this disorder. This is suggested by the demonstrated potency of this gland in stimulating follicle maturation, and, under certain conditions, of preventing ovulation by imprisonment of the ova within the follicles. Varying effects are produced by varying proportions of the two hormones which, according to the work of Evans and Simpson,[32] are produced by the gland, and it is quite possible that some disturbance of the normal balance between these two principles is the underlying cause of this type of hemorrhage, especially in view of the ovarian picture that characterizes it.

The second recent development is the successful elaboration, by Corner and Allen,[5] of a really potent corpus luteum extract. Whatever the underlying cause of functional hemorrhage may be, a characteristic ovarian finding is an absence of corpora lutea. The administration of an active corpus luteum extract would therefore be a rational procedure. Thus far no such extract has been available, but, if the work of Corner and Allen results in making such an extract available for clinical use, there is reason to hope that the organotherapy of functional hemorrhage of this type will be more successful than at present. There is, of course, no certainty of this, for there are still many unknown links in the menstrual chain. The use of such an extract, however, should certainly be tried, for this type of bleeding, especially when it affects women in whom preservation of the reproductive capacity is important, constitutes one of the most difficult present-day problems in gynecology.

The employment of hypodermic treatment for this type of pathologic hemorrhage does not possess the disadvantages mentioned in discussing hypodermic medication in cases of amenorrhea, especially as the former is a seriously debilitating disorder. The alternative of organotherapy is usually surgical operation or radiotherapy, both undesirable in younger women. If, therefore, an extract is made available which controls this type of bleeding, it will confer an inestimable boon to patients suffering with this troublesome disorder.

SUMMARY

Recent advances in knowledge of the physiology of menstruation make it necessary to revise the interpretation of the mechanism involved in functional menstrual disorders, and, of course, have a bearing on problems of treatment as well.

Amenorrhea and hypomenorrhea (scanty menstruation) are most often of constitutional or endocrinopathic origin, local pelvic causes being much less common. The ovarian function is singularly sensitive to nutritional and circulatory deficiencies, disappearance of the cycle being the common result. The treatment of the amenorrhea produced by such general diseases as tuberculosis, anemia and dietary deficiencies is, of course, the treatment of the underlying conditions, and endocrine therapy is contraindicated.

Of the endocrine causes of amenorrhea the most common are ovarian deficiency, hypopituitarism and thyroid disorder, most often hyperfunction, but at times hypofunction. These types are often distinguished by fairly well defined clinical syndromes, such as the adiposogenital dystrophy of hypopituitarism, but the scientific basis for such differentiation is often incomplete.

Amenorrhea is often unaccompanied by other symptoms and may need no treatment except reassurance of the patient as to the essential harmlessness of the condition. In other cases, as when it is subordinated to the accompanying sterility, efforts at treatment are

27. Rubin, I. C.: Am. J. Obst. & Gynec. **12**: 76 (July) 1926.
28. Rongy, A. J.: Am. J. Obst. & Gynec. **13**: 598 (May) 1927.
34. Novak, Emil, and Martzloff, K. H.: Am. J. Obst. and Gynec. **8**: 385 (Oct.) 1924. Novak, Emil: The Treatment of Functional Uterine Hemorrhage, J. A. M. A. **86**: 1105 (April 10) 1926.

indicated, though unsuccessful in a large proportion of cases.

The three organ extracts that are commonly employed are those derived from the ovary, the anterior pituitary and the thyroid, in various combinations. The oral administration of ovarian extracts is worthless, as far as any effect in the reestablishment of menstruation is concerned. The same statement probably applies to the older forms of preparations for hypodermic administration. Ovarian follicle hormone, more recently employed, has so far yielded no worth-while therapeutic results, important as it is physiologically. The recent discovery of an active corpus luteum principle may improve the results somewhat, but these will still be far from ideal, as neither of the principles named apparently has any stimulating effect on the ovary itself.

The treatment of amenorrhea by means of the anterior pituitary suggests itself as offering the best hope for the future, because of the striking effect on the follicle apparatus produced by the hormone of this gland. If the latter is made available for clinical use in some convenient form, its employment in certain cases of amenorrhea and sterility will be rational, although perhaps even with this the results may be disappointing. The oral administration of pituitary substances is probably without value. For the present, thyroid therapy, at times on rational indications, at times on empiric or semiempiric grounds, is still the most popular and perhaps the most frequently helpful plan in most cases.

Not much can be added as to the treatment of too frequent or too infrequent menstruation (polymenorrhea or oligomenorrhea) because of ignorance as to the nature of the factor or factors that normally regulate the menstrual rhythm. The treatment of oligomenorrhea is in general similar to that of amenorrhea and hypomenorrhea.

Excessive menstruation of functional nature (hypermenorrhea) is an extremely frequent and important disorder, especially in women at or near the menopausal age, because of the fact that, like other types of bleeding at this age, it calls for differentiation from that produced by cancer. For a discussion of this disorder the reader is referred to several previous papers. When potent corpus luteum extracts, such as that demonstrated recently by Corner and Allen, become available commercially, their employment in this condition will be rational and may possibly yield excellent results.

Some such system of nomenclature of menstrual disorder as that employed in this paper would seem worthy of general adoption. This would simplify records and indexes materially, through the elimination of such clumsy and circumlocutory terms as "too frequent menstruation," "deficient amount of menstruation," and the like. Various systems of naming these disorders have been suggested, but the one that seems most logical is as follows: amenorrhea, for the absence of menstruation; hypomenorrhea, for a deficient amount of the menstrual discharge; hypermenorrhea, for an excessive menstrual flow; oligomenorrhea, for too infrequent menstruation; polymenorrhea, for too frequent menstruation; dysmenorrhea, for painful menstruation. Various combinations of these terms are at times called for, and would be self-explanatory; viz., oligohypomenorrhea; oligohypermenorrhea, polyhypermenorrhea, and so on.

While the organotherapy of menstrual disorders is still unsatisfactory, the recent additions to our knowledge of the physiology of the sex cycle justify the hope that before long the problem can be approached much more intelligently and precisely than in the past. It would seem quite likely, for example, that the etiology of the various disorders will soon be determinable by studies on the biologic chemistry of the blood. In other words, just as quantitative determinations of blood sugar or blood urea can now be made, it will perhaps be possible to determine deficiency or excess of such principles as the ovarian follicle hormone, the anterior pituitary or thyroid secretions. These methods of course have already been used to some extent, but their refinement, simplification and wider utilization may make of organotherapy a more scientific procedure than it has been in the past.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. ROWE AND NOVAK

DR. J. P. PRATT, Detroit: The problem is indeed complex, for the human sexual cycle is so different from the estrous cycle of animals that it is hazardous to draw conclusions from animal experimentation until there has been a complete check in the human subject. The suggestion to adopt a standard terminology is timely. Confusion in the literature would be avoided. Function of the ovary, like other endocrine glands, is either normal, hypo or hyper. Reference to the function of the glands with internal secretion as a "chain of glands" or as being interrelated seems confusing. Would it not be better to think of each tissue or gland as composed of cells which have the ability to take out of the circulation and to utilize materials in a manner characteristic of the tissue or cell? The thyroid, for example, puts into the circulation a hormone which is a definite chemical substance. This is carried to all parts of the body by the blood. Each tissue or organ may utilize this hormone according to the ability of the individual cells to respond to it. The same is true of the other elements of the blood, such as iron or calcium. Thus in the case of the ovary and uterus, if the blood circulating through them does not contain a sufficient quantity of iron or calcium, or hormone of any of the various glands of internal secretion, the activity of the ovary or uterus will be affected accordingly. Since the hormones isolated from the various glands of internal secretion are definite chemical compounds, disturbances of function of these glands are either hypofunction or hyperfunction. In line with this interpretation it would seem that disturbances of function of the ovaries and uterus are due to too much or too little of some material in the circulating blood. However, not all instances of disturbed function are due to a deficiency of the same material; therefore the intelligent treatment of disturbance of menstruation would necessitate determining the lack or oversupply of the material responsible for the abnormality in each individual case. Until such methods of analysis of the blood are discovered, treatment will have to be continued empirically. As suggested, one of the best therapeutic agents for ovarian deficiency is thyroid. This apparently acts on the ovaries directly. I cannot share Dr. Novak's pessimism in reference to treatment of ovarian deficiency by the use of ovarian follicular hormone, for I have followed a small group of cases for a few years in which the combination of thyroid and ovarian follicular hormone has relieved oligomenorrhea and hypomenorrhea.

DR. CAREY CULBERTSON, Chicago: I take it that the menstrual irregularities which are of the greatest interest are those occurring in young women. Physicians are not so much concerned with the menstrual disturbances of the older woman who is approaching the climacteric, because an amenorrhea is expected at that time, and the treatment for excessive bleeding in those years is well known. It is in the young women who suffer from amenorrhea, irregular menstruation and excessive bleeding, whatever name is given it—I myself like the terms which Dr. Novak has suggested, and have used them—also in the young women who suffer from dysmenorrhea, that the interesting problems are presented at this time, chiefly because

dysfunction is not understood. I am curiously impressed in hearing Dr. Novak's paper by the fact that he makes no reference to the suprarenal glands. When I first began to study the endocrines twenty years ago, I had an idea, based on the work done then by Hoskins and others, that the suprarenals had a great deal to do with ovarian function. Today it is the anterior pituitary and the thyroid influence that is chiefly discussed, but more regarding the suprarenals may yet be heard. The ovary still seems to be, as I have thought of it for some years, an organ that requires stimulation in order to keep it functioning. But this evidently is true of the others as well. Where the stimulation comes from is the interesting thing, and how it is applied. Until that is known, ovarian dysfunction cannot be treated satisfactorily. Just as in studying the climacteric, so in studying these functional disorders of younger women one cannot get away from either the pituitary or the thyroid gland. That is the reason recourse has had to be made frequently, as Dr. Novak mentioned, to basal metabolic and to blood pressure studies. In this connection, I should like to emphasize that one blood pressure reading, one basal metabolic rate estimation is not enough. One has to make repeated estimations of metabolism and of vascular tension in order to understand best the condition to be treated. Theoretically, since the anterior lobe of the pituitary gland seems to be most influential in ovarian function, hypophyseal preparations should be of definite therapeutic aid, particularly in the amenorrheas. Such preparations as are offered, however, have been disappointing. An occasional case may appear to be benefited, but the majority are not.

DR. EMIL NOVAK, Baltimore: I am afraid that the trend of my paper has seemed much more destructive than constructive. I wish it could be otherwise and that I could suggest some simple and more or less infallible way of curing these functional disorders, but the limitations of this field must be, and should be, admitted. If there is to be advance, the weeds and underbrush must first be cleared away. Dr. Pratt believes he has had good results with the ovarian follicle hormone in some cases of disturbance of menstrual rhythm, although he said nothing as to its use in amenorrhea, which has been supposedly its chief field. As I stated in my paper, we know little as to the cause of menstrual irregularity. When it is moderate in degree, as when a woman menstruates every three weeks or every six weeks, it appears to make little difference to the patient. Thyroid extract is still perhaps the most frequently useful therapeutic agent in cases of amenorrhea, especially when obesity is associated with it. I have elaborated on this in my paper, which I presented only in abstract. There is much reason to feel enthusiastic about the future possibilities of gynecologic organotherapy but not much to inspire pride as to its accomplishments up to the present time.

"The Sleepy Arteries."—On what grounds the tortuous intracranial segments of the internal carotid arteries, whose branches enter the rete mirabile, came to be called "the sleepy arteries" is lost in antiquity, but for some reason or other the idea has prevailed that the function of sleep was ascribable to this region. There seemed to be something more in the idea than pure conjecture, but just what the mechanism of sleep and its alternate phase of waking might be was undetermined. Among theories innumerable, that there may actually be a diencephalic center for the process has been claimed, and the recent demonstration by Hess (1929) of a definite hypothalamic area in the cat stimulation of which will promptly induce a condition which is indistinguishable from sleep points suggestively in this direction. Then, too, we have had before us, these past fifteen years, the all too common examples of lethargy associated with encephalitis, a malady whose effects are prone to strike at this particular part of the brain as shown by other symptoms unmistakably hypothalamic in origin. . . . Thus it would appear that pathological sleep, and conversely of course abnormal wakefulness, in all probability are states induced by a disordered function of the hypothalamus.—Cushing, Harvey: Neurohypophysial Mechanisms from a Clinical Standpoint, Lister Memorial Lecture, *Lancet*, July 26, 1930.

ATROPHY OF THE LIVER DUE TO CINCHOPHEN PREPARATIONS*

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Except for the report of a case of atophan hepatitis by Worster-Drought [1] in 1923 and a fatal case of liver atrophy due to Weldona tablets demonstrated by Cabot [2] in 1925, actual knowledge of the toxic effect of cinchophen preparations on the liver dates from 1926. In a little more than four years, forty-one cases have been reported. Including my two cases previously reported and seven cases presented here, there is a total of fifty cases with twenty-five deaths and twenty autopsies, confirming the diagnosis of toxic hepatitis and liver atrophy as the cause of death.

It is highly probable that many cases have not been reported, and that many more cases of jaundice and liver atrophy would on careful investigation prove to be due to the previous use of the drug in one of its forms. This has been amply demonstrated by my own experience. The association of a jaundiced state or atrophy of the liver with the use of cinchophen preparations can no longer be considered a mere coincidence.

The discovery of the preceding use of a cinchophen preparation is the only diagnostic point, since symptomatology and pathology in no wise differs from similar parenchymatous damage of other causation. Toxic symptoms may arise while taking the drug or as late as two months after cessation (Cabot). Suspicion must always arise when questioning reveals previous suffering from joint, muscle or nerve pain. It is in the latter conditions that cinchophen preparations are being so much used. As a result of the extensive advertising claims as a safe analgesic, these preparations are being indiscriminately dispensed in tremendous amounts over the drug counter on request of the layman. Nothing can be further from correct than Hanzlik's [3] statement that, "since the [toxic] symptoms of cinchophen and its ethyl ester and neocinchophen are identical with those of salicyl, no further description is necessary," or Barbour, Lozinsky and Clements' [4] opinion that cinchophen appears to be devoid of side-actions.

CHEMISTRY

Cinchophen, chemically 2-phenyl-quinoline-4-carboxylic acid, was introduced about 1908. Rotter [5] states that it is excreted in the urine as hydroxyl-phenyl-quinoline-carboxylic acid and is therefore not decomposed in the body but excreted after slight oxidation. According to Willcox,[6] the toxic action arises from the quinoline nucleus, consisting of the benzene and the pyridine rings, which yield the toxic ring of free benzene. It is known that atoquinol, arsphenamine and trinitrotoluene all contain the benzene ring and are all capable of producing liver atrophy. Sollmann [7] says that benzene is relatively resistant to decomposition, only a little being oxidized and forming phenols and acids. Sutton [8] states that neither benzene nor phenol produces jaundice in overdoses, but that the nitrophenols (dini-

* Read before the Section on Practice of Medicine at the Eighty-First Annual Session of the American Medical Association, Detroit, June 25, 1930.

1. Worster-Drought, C. C.: Brit. M. J. **1**: 148 (Jan. 27) 1923.
2. Cabot, R. C.: Boston M. & S. J. **192**: 1122 (June 4) 1925.
3. Hanzlik, P. J.: Medicine **5**: 349 (Aug.) 1926.
4. Barbour, Lozinsky and Clements: Am. J. M. Sc. **165**: 708 (May) 1923.
5. Rotter, L.: Chem. Abstr. **12**: 2384, 1918.
6. Willcox, W. H.: Brit, M. J. **2**: 273 (Aug. 7) 1926.
7. Sollmann, Torald: Manual of Pharmacology, ed. 2, Philadelphia, W. B. Saunders Company, 1922, p. 569.
8. Sutton, D. C.: Acute Yellow Atrophy of the Liver Following the Taking of Cinchophen, J. A. M. A. **91**: 310 (Aug. 4) 1928.

trophenol, trinitrophenol or picric acid) and the nitrobenzenes (nitrobenzol and trinitrotoluene) all produce liver damage. He further believes that the liver is concerned in the decomposition of these products and that under certain conditions the oxidation of the quinoline nucleus produces highly toxic nitro compounds.

PREPARATIONS

Phenyl-cinchoninic acid, atophan, novatophan, atophanyl, diiodoatophan, biloptin, oxyliodide, quinophan, agotan, neo-cinchophen, phenoquam, leucotropin, atophan-urotropine, fantan, iriphan, tolysin, weldona and farastan are all congeners of cinchophen. Atoquinol (atochinol) is a derivative of cinchophen.

PATHOLOGIC AND CLINICAL PICTURES

The amount of degeneration and compensatory regeneration of liver tissue varies with each individual case, thereby producing different clinical pictures. Transitional stages between reversible and irreversible liver damage are possible. So-called catarrhal jaundice has been shown by Eppinger and others to be mild hepatitis ending in recovery. When greater degeneration, necrosis and destruction of liver cells occurs, the condition might be called hepatolysis. When the destructive process is quite extensive, it might be spoken of as liver atrophy. For a more complete description of the various pathologic and clinical pictures under discussion, the reader is referred to my [9] original paper on toxic hepatitis following the use of atophan. These pathologic and clinical states probably do not differ in any way from similar states due to other etiologic factors, and depend entirely on the relative amount of atrophy, regeneration, cirrhosis and nodular hyperplasia. With longer duration, opportunity for regeneration with cirrhosis and nodular hyperplasia is given. There is great tendency to development after tonsillectomy and to fatality soon after exploratory laparotomy, due to surgical trauma, anesthesia and enforced starvation. Clinically there is no evidence of malignant neoplasm. Common bile duct stone is easily excluded when jaundice appears without pain and there is no past history of indigestion or colic. Knowledge of the selective affinity of cinchophen for the liver, the history of its use, and the absence of any other cause for the appearance of jaundice suggests the diagnosis. Numerous postmortem studies have established the truth of these statements.

CASES REPORTED IN THE LITERATURE

A man,[1] aged 59, received 18 Gm. of atophan during twelve days. When he developed urticaria, he stopped the drug for three weeks; then after again taking 0.5 Gm., he developed urticaria the next day and jaundice ten days later which lasted several weeks with recovery. This is the first case to be described in the literature.

A man,[2] aged 42, took three packages of weldona during six months. Two months later the patient had pains, colic, jaundice and indigestion. A physical examination revealed the liver just palpable, bile in the urine in five out of seven examinations, clay colored stools and a negative Wassermann test. Roentgenograms were practically negative. The liver became smaller; ascites, some edema, hematemesis and pigmentation developed. There was no fever. The patient died three months later. Cabot mentions "having had an extraordinary series of cases of acute yellow atrophy in patients who have been taking this medicine called weldona." Postmortem examination revealed: acute toxic atrophy of liver, slight secondary cirrhosis, gastro-esophageal varices, ascites, hydrothorax, left serofibrinous pleurisy, edema of the legs and hemorrhages. This case has escaped the attention of those who have hitherto written on this subject. According to advertisements, weldona is stated in THE JOURNAL to contain neocinchophen, magnesium carbonate and cascara.[10]

A woman,[11] age not stated, took 5 cc. of atophanyl intravenously fifteen times; she stopped for three days, then took 0.5 Gm. of atophan three times daily for a month. She stopped the drug by mouth because of indigestion, then took some more injections followed by 0.5 Gm. of atophan twice daily for one month—a possible total of 83 Gm. Jaundice occurred, with recovery in several weeks. Not aware of Worster-Drought's and Cabots' cases, Klinkert erroneously believed his to be the first case of liver damage to be reported.

A woman, aged 55, took 70 Gm. of atophan, developed marked urobilinuria without jaundice, and recovered in four weeks. This case does not properly belong in this series, since the author is tabulating only severe cases of toxic action on the liver—such as have developed jaundice.

Langdon-Brown [12] reports two deaths due to atoquinol and states that he knows of two other fatal cases. Atoquinol is chemically allyl-phenyl-cinchonin ester and, though differing materially from atophan, contains the same toxic principle.

Graham [13] gives the details of these two deaths reported by Langdon-Brown. A woman, aged 69, took 12 Gm. of cinchophen weekly for ten weeks. She developed anorexia, vomiting and jaundice; some bile was found in her stools. The patient died the eighth day after admission to the hospital. An autopsy was performed. The other patient was a woman, aged 36, who took 130 Gm. of atoquinol within a period of five months. She stopped for one month and then took 22 Gm. The patient developed jaundice and died in ten days. There was no autopsy.

Evans [14] reports three cases, the age and sex not stated, due to atophan, each patient receiving about 15 Gm.—one case occurring on two separate occasions, once after only 1 Gm. All the patients recovered. He states that all preparations are equally toxic.

Glover [15] reports a case developing after ten atophanyl injections. The patient recovered.

A man,[16] aged 69, received 6 Gm. of atophan inside of one week. A few days later he became jaundiced. He was ill twenty-eight days and died. There was no autopsy. Willcox mentions, without giving any data, two other cases with recovery.

A woman,[17] aged 63, took 200 Gm. of atophan during four and one-half months. After she had been taking the atophan for three months she developed vomiting, and later jaundice. She died in coma on the tenth day of the jaundice. A postmortem was held.

A man,[18] aged 60, took 80 Gm. of atophan inside of two and one-half months. He developed ascites; he was ill three months and recovered.

A woman,[19] aged 31, received an intravenous injection of 5 Gm. of diiodoatophan (biloptin, 50.7 per cent iodine) for cholecystography, cholecystectomy for cholelithiasis and chronic cholecystitis next day. There were no stones in the hepatic or common bile duct and no injury to the common bile duct. The patient developed jaundice two days later; she was ill twenty-six days and discharged with slight jaundice and advanced anemia.

A woman,[20] aged 21, received an intravenous injection of diiodoatophan, developed toxic hepatitis the same day, and died ten days later. A postmortem was held.

A man,[20] aged 60, received diiodoatophan; toxic symptoms developed the next day. The patient recovered.

A patient [21] received diiodoatophan; toxic symptoms developed the next day. The patient recovered.

9. Rabinowitz, M. A.: M. Clin. North America **11**: 1025 (Jan.) 1928.

10. Weldona: A Piece of "Rheumatism Cure" Quackery, J. A. M. A. **89**: 1167 (Oct. 1) 1927.
11. Klinkert, D.: Therap. d. Gegenw., July, 1926.
12. Langdon-Brown, W.: Brit. M. J. **2**: 37 (July 3) 1926.
13. Graham, George: Proc. Roy. Soc. Med. **20**, 1926-1927, part 3, Section Therap. and Pharmacology, p. 258.
14. Evans, Geoffrey: Brit. M. J. **2**: 93 (July 10) 1926.
15. Glover, L. G.: Brit. M. J. **2**: 136 (July 17) 1926.
16. Willcox, W. H.: Brit. M. J. **2**: 273 (Aug. 7) 1926.
17. Wells, C. J. L.: Brit. M. J. **2**: 759 (Oct. 23) 1926.
18. Klinkert, D.: Klin. Wchnschr. **6**: 24 (Jan. 1) 1927.
19. Kingreen, O.: Deutsche med. Wchnschr. **53**: 971 (Jan. 28) 1927.
20. Hitzenberger, H.: Wien. Klin. Wchnschr. **40**: 205 (Feb. 17) 1927.
21. Schwartz, G.: Wien. Klin. Wchnschr. **40**: 238 (Feb. 17) 1927.

A woman,[22] aged 56, received diiodoatophan; symptoms developed the same day. The patient died. A postmortem was held.

A man,[23] aged 32, received diiodoatophan; toxic symptoms developed two days later. The patient recovered.

A man,[24] aged 54, took atophan in large amounts for a long period; after one month toxic symptoms developed. A laparotomy revealed no gallstones. There was atrophy and cirrhosis of the liver. Death occurred two days later. An autopsy was held.

A woman,[25] aged 52, was given 18 Gm. of atophan. When jaundice developed, the drug was stopped. Another physician represcribed atophan and the jaundice reappeared. The illness lasted six weeks. The patient recovered.

Toxic symptoms developed in a patient [25] after several tablets of atophan were taken. The patient recovered after an illness of forty days.

A woman,[25] aged 52, took forty-eight tablets of atophan. She recovered.

A man,[9] aged 33, took about 15 Gm. of atophan during five months. He recovered after an illness of three months.

A man,[9] aged 39, took 13 Gm. of atophan during about ten days; he was ill four weeks and recovered.

A man,[26] aged 47, took atophan, the amount and duration not stated, and died of acute yellow atrophy. An autopsy was held.

A woman,[27] aged 65, took a total of 60 Gm. of atophan within four weeks. Jaundice developed; she recovered in five weeks.

A woman,[28] aged 55, took large doses of atophan during six months. Jaundice appeared two weeks after the drug was stopped; the illness lasted one week, terminating in death. An autopsy was held.

A woman,[28] aged 55, took atophan for periods of three days with four day intervals, together with sodium bicarbonate during eight weeks. After an illness of five weeks the patient died. An autopsy was held.

A woman,[29] aged 55, took an atophan tablet three times daily for three weeks and died of acute yellow atrophy of the liver. The case came to a coroner's inquest. Mention is also made of another case of acute yellow atrophy due to atophan reported two months previously at the Liverpool Medical Society.

A woman,[18] aged 27, took at least seventy-five tablets of cinchophen over an unstated period, developed nausea, vomiting, constipation, urticaria, jaundice, small liver, ascites and died two and one-half months after the onset of jaundice following a Talma operation. A postmortem was held.

A woman,[30] aged 29, unmarried, took salicylates and atophan tablets. During this time she developed angina complicated by phlegmon from which she recovered without operation. Jaundice developed at the end of three weeks of atophan usage, with recovery at the end of one month.

A woman,[31] aged 27, took a total of 117 Gm. of cinchophen in two periods during two months. Jaundice disappeared after two months.

A woman,[32] aged 45, received atophanyl intravenously during a period of twenty-five days, followed nineteen days later by progressive jaundice, bile in the urine, enlarging liver, icteric index as high as 120 and later ascites. The patient recovered after a three months' illness.

A woman,[33] aged 37, suffered with toxemia in a previous pregnancy, followed by a run-down condition and aches. After about one year of an undetermined amount of atophan, indigestion and pruritus developed; two weeks later jaundice, epigastric and lumbar pain developed. Jaundice rapidly cleared up in three weeks. A cholecystogram was negative. Ten weeks later there occurred indigestion, vomiting, a slight ache in the epigastrium, jaundice, pruritus, erythema, enlarged spleen and fulminating toxemia. The patient died nineteen days later. A postmortem disclosed acute yellow atrophy.

A man,[34] aged 55, given only 6 Gm. of atophan within two days was ill three weeks. He recovered.

A woman,[35] aged 48, took 600 tablets of oxyl iodide (each tablet is 3 grains [0.2 Gm.] and contains 83.3 per cent cinchophen) during a period of seven months. Death from acute yellow atrophy after an illness of nine days was revealed by a postmortem examination.

A woman,[36] aged 20, took cinchophen since January; jaundice developed in May, a week after tonsillectomy, and lasted six weeks. With the recurrence of arthritis, large doses of cinchophen plus oxyiodide were given followed by fever, purpura, enlarged liver and enlarged spleen. The patient died. Postmortem examination revealed toxic cirrhosis of the liver.

A woman,[36] aged 46, repeatedly took large amounts of cinchophen over a period of three years. Death occurred on the tenth day after the onset of jaundice and cholemia. An autopsy was held. Reichle states that at the conference in the City Hospital in which one of his cases was presented, several physicians reported that they had seen jaundice during the period of medication with cinchophen.

A woman,[37] aged 52, had an epithelioma of the cervix of the uterus which extended onto the posterior vaginal wall. Radium treatments were given. From 1923 to 1929 the patient enjoyed excellent health. During the summer of 1929 she suffered with neuritic pains in the right thigh for which she took from one to three tablets of cinchophen daily for six weeks. She finally discontinued the medicine because of the appearance of nausea and vomiting, which developed one month after she had begun to take the drug. A week after she had stopped taking cinchophen, jaundice appeared suddenly, concomitantly with an attack of diarrhea which lasted only a day. The jaundice was intense from the beginning and did not fluctuate. There was no purpura or pruritus. Her condition grew steadily worse and she died sixteen days after the onset of the jaundice, with terminal hyperpyrexia and signs of bronchopneumonia. At postmortem examination the liver weighed only 903 Gm. Obstruction of the right ureter with hydronephrosis, was present, as the result of the previous malignant condition.

ADDITIONAL CASES

CASE 1.—L. C. K., a woman, aged 37, whose father suffered from asthma, had had one pregnancy followed by hysterectomy for uterine fibroids nine years before. She had had aches and pains particularly in the feet for four years, and she was overweight. Her basal metabolism was —10. She was prescribed thyroid, ½ grain (0.03 Gm.), and cinchophen, 2 grains (0.13 Gm.), three times daily, which she took on and off without untoward results for two months. Basal metabolism was then —6, fasting blood sugar 79 mg. per hundred cubic centimeters. Thyroid, ⅔ grain, (0.04 Gm.) and cinchophen, 2 grains, three times daily were then given. One week later she felt tired and languid; two and one-half weeks later her urine became dark, soon to be followed by jaundice with itching. The liver was palpable, and she had lost 12 pounds (5.4 Kg.) in the last three months. The spleen was never palpable. The gallbladder a short time previously had been negative to cholecystography. On a high carbohydrate diet with insulin injections, jaundice rapidly disappeared; the liver was no longer palpable. The illness lasted about two months. The patient recovered and has remained well.

CASE 2.—(service of Dr. Adolph Bonner, Jewish Hospital)—A woman, aged 31, had had asthma and hay-fever a year before she was seen, for which she received desensitizing injections. One month before admission she had a febrile upper respiratory infection which was followed by aches and pains in the back and shoulders, for which she was advised a 7½ grain (0.5 Gm.) tablet of atophan three times daily; she took a total of 20 tablets. In a few days after beginning the drug she

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33. McVicar, C. S., and Weir, J. F.: M. Clin. of North America **12:** 1526 (May) 1929.
34. Frenzel, W. C.: Wisconsin M. J. **28:** 264 (June) 1929.
35. Anderson, S. D., and Teter, D. P.: Acute Yellow Atrophy of the Liver Following Administration of Oxyl Iodide, J. A. M. A. **93:** 93 (July 13) 1929.
36. Reichle, H. S.: Toxic Cirrhosis of Liver Due to Cinchophen, Arch. Int. Med. **2:** 281 (Aug.) 1929.
37. Stacy, L. J., and Vanzant, F. R.: Minnesota Med. **13:** 281-367 (May) 1930.

developed weakness, followed in about two weeks by jaundice and dark urine containing a trace of sugar. She was admitted to the wards. The liver edge was 4 cm. below the right costal margin. Jaundice and itching became marked; there was no fever. The stools were clay colored but showed traces of bile from time to time; the icteric index was 70 on admission; a tetraphenolchlorophthalein test for the liver damage was positive. The blood Wassermann reaction was negative. Fasting blood sugar was 100 mg. per hundred cubic centimeters. Urine bile was present. There was no leucine or tyrosine. The gallbladder could not be visualized by intravenous injection of dye. No colics occurred. On admission, menstruation was overdue one week. The uterus gradually enlarged. A diagnosis of pregnancy was made, and because of her hepatic condition, therapeutic abortion was done. An examination of the curettings showed that pregnancy was present. Jaundice gradually cleared up, and she was discharged completely recovered in seven weeks.

CASE 3.—(service of Dr. Soresi, Greenpoint Hospital).—G. C., a man, aged 45, suffered from generalized aches and pains for one month. Atophan was begun, Sept. 30, 1927, with a dosage of one tablet of 7½ grains three times daily. Feb. 8, 1928, four months later, this dosage was increased to a tablet every three hours. During this period (October 21, 25, November 2, 9, 21 and December 28) he had also received six injections of 5 cc. of Lactogen—a sterilized milk preparation—as parenteral protein therapy. December 28, the injection was followed by shock and he was admitted to the hospital and discharged the next day with the advice to continue the atophan. February 17, it was noted that the patient was very weak and at times he became unconscious for as long as three quarters of an hour. He had lost 55 pounds (25 Kg.) in the last year, suffered epigastric pressure, and was markedly jaundiced for four days. He was readmitted to the hospital. Ascites and hydrocele were present; the urine showed bile; the blood count was 19,000 white cells, of which 80 per cent were polymorphonuclears. There was no fever. The patient died six days later, and postmortem examination revealed normal pancreas, gallbladder and biliary passages. The liver weighed 1,100 Gm., showed marked pericapsular adhesions, cut with resistance, and on section revealed nodular hyperplasia with portal cirrhosis. There was no evidence of cholangeitis. The spleen weighed 225 Gm. and was normal. There were patches of purulent peritonitis.

The following case reports, heretofore unpublished, are from the service of Dr. Leo Kessel [38] of Mount Sinai Hospital, New York, Dr. Max Grolnick [39] and Dr. A. A. Stone [40] of Brooklyn, to whom I am indebted for the privilege of presentation and publication at this time.

CASE 4.—(service of Dr. Leo Kessel [38]).—C. K., a woman, aged 51, complained of epigastric distress after meals for the past year, relieved by sodium bicarbonate; she tired easily, was markedly constipated, and suffered from severe pain in both knees, which became worse on motion. The diagnosis was chronic infectious arthritis, nasopharyngitis, infected tonsils and obesity. A tonsillectomy was performed, March 1, 1929. She was put on sodium salicylate and iodides, and atophan 5 grains (three times a day?) with instructions to take the prescription until the pain ceased. At a subsequent visit the medication was renewed. After four weeks the patient was bedridden and jaundiced. For two days there was severe abdominal pain in the right upper quadrant and epigastrium. She was admitted to the hospital, April 20. The last four days she had been restless and her eyes were glazed. There was twitching, followed by coma of twenty-four hours' duration. The patient was comatose and deeply jaundiced, with pitting edema of the ankles, and the liver was small to percussion. A provisional diagnosis of acute yellow atrophy of the liver was made. The blood count was: hemoglobin, 85 per cent; red blood cells, 4,700,000; polymorphonuclears, 90 per cent; platelets, 300,000; bleeding time, three minutes, and coagulation time, two minutes. A tourniquet test was negative. The blood pressure was 95 systolic and 50 diastolic. She died within twenty-four hours after admission. The autopsy observations were: subacute yellow atrophy of the liver, jaundice, edema of the ankles, parenchymatous degeneration of the heart and kidneys, tracheitis and bronchitis, obesity and hemorrhages in the skin and mucous membranes of the intestine, trachea and bronchi.

CASE 5. (service of Dr. Leo Kessel [38]).—W. W., a patient, aged 26, married, after having constant indefinite complaints for two years, developed six weeks before admission a fleeting speckled rash, migratory polyarthritis, slight fever, chilliness and slight precordial pain. Cough developed three days before admission. Examination revealed good nutrition, infected tonsils and slight fever; the spleen was enlarged 3 fingerbreadths below the costal margin; the liver felt 1 fingerbreadth below the costal margin; there was no swelling or tenderness of the bones or joints; there were a few erythematous areas over the face, chest, hands and anterior area of the elbows, and there was a diffuse generalized lymphadenopathy. The blood count was: white blood cells, 11,700; polymorphonuclears, 82 per cent. Mellitensis agglutination and blood cultures were negative; a roentgenogram of the chest showed no abnormality; the urine on admission was negative. Atophan was given to relieve the joint pains, the patient receiving about 70 grains (4.5 Gm.) in all. Tonsillectomy was performed, followed by sudden jaundice, fever and a poor general condition. A liver function test showed a dye retention of 100 per cent in thirty minutes; the sedimentation time was two hours. The temperature rose to 105 F. and the patient died ten days after the onset of the jaundice, in spite of high carbohydrate diet and repeated infusions of dextrose. It was felt that the temporary deprivation of food preceding the tonsillectomy was a factor in making the liver more susceptible to the effect of the atophan.

May 29, 1930, Dr. Kessel, two of whose cases have been reported, wrote: "I have seen a total of thirteen cases of atophan poisoning."

CASE 6 (patient of Dr. Max Grolnick [39]).—A woman, aged 45, who had never been pregnant and had suffered numerous infections, especially of the upper respiratory tract and the genitalia, developed arthritic pains for which she took weldona tablets. This was followed by backache. Two weeks later she again took six weldona tablets, followed the next day by backache, epigastric distress, bile in the urine, jaundice and clay-colored stools. The taking of these tablets had been preceded by intravenous injections of "some preparation made from the joint fluid" by another physician. Examination revealed obesity and jaundice. There was no fever. The liver was tender but not enlarged. There was bile in the urine; the stools were acholic; red cell hemolysis began at 0.32; the icteric index was 57. A Wassermann test was negative; gallbladder visualization was at first negative; after recovery it was normal. There was a rapid improvement and the patient was discharged in five weeks.

CASE 7 (patient of Dr. A. A. Stone [40]).—A woman, aged 39, treated for six months with large doses of atophan for arthritis of the hip, developed progressive jaundice. An exploratory laparotomy was done and the patient died on the table after an illness of four months. Very small cirrhotic atrophy of liver (gross and microscopic) was found.

PREDISPOSITION

I believe that only under certain conditions does the liver become sensitized to the toxic action of the cinchophen preparations. The duration of its use and the total amount ingested or otherwise introduced into the body have been found to vary in each case, one person developing ill effects after a comparatively small amount, intravenously or by mouth, while another may not develop it until after long continuous use. De Rezende's second patient received only about 3 Gm., one of Kessel's patients, 4.5 Gm.

Predisposed are those with gallbladder disease, cirrhosis of the liver, pregnancy, chronic alcoholism, chronic nephritis, those who in the past have suffered

38. Kessel, Leo: Personal communication to the author, May, 1929.
39. Grolnick, Max: Personal communication to the author, May, 1929.
40. Stone, A. A.: Personal communication to the author, May, 1929.

from liver disease associated with jaundice, and those showing other evidences of cinchophen intolerance. The drug appears particularly dangerous in states of hepatic damage accompanying starvation, malnutrition, cachexia, chronic infection or tonsillectomy, after fevers, or in conditions favoring decreased glycogen content of the liver cells. Unger and others have definitely proved that under these conditions there is greater tendency to liver degeneration. Cinchophen, according to Taubmann,[41] is excreted in the bile and inhibits carbohydrate digestion, thus further favoring decreased liver glycogen storage.

A closer study leads to the suspicion that sensitization of the liver to protein, whether by surgical trauma, inhalation, ingestion, or parenteral injection (milk preparations such as lactogen and aolan or vaccines) renders it most susceptible to the toxic damage of cinchophen. Experiments are now under way to determine this point.

PRECAUTIONS

In spite of all the precautions hitherto advised, cinchophen therapy has proved dangerous. Intermittent use to avoid retention of dangerous amounts proved of no avail in cases reported by Klinkert, Langdon-Brown, Lowenthal and myself. Neither the associated intake of large amounts of fluid to aid more rapid elimination nor the use of large doses of sodium bicarbonate are certain guarantees. Large amounts of readily assimilable carbohydrates, given with small amounts of insulin, might protect the liver by restoring its glycogen content. It has been proved that carbohydrate without insulin is insufficient for this purpose. The intravenous use of cinchophen appears dangerous.

EARLIEST SIGNS OF TOXICITY

The drug should best not be used in ambulatory cases, as the earliest signs are thus likely to be overlooked. These warning signs are malaise, anorexia, nausea, vomiting, indigestion, pruritus, urticaria, albuminuria, pains about the liver, subicterus, tenderness of the liver, rise in the bilirubin content of the blood, bile pigment in the urine, marked urobilinuria, marked depression of the vasomotor system, purpura, scarlatiniform rash, or edema with fever.[42]

TREATMENT OF LIVER DAMAGE

With the earliest appearance of toxic phenomena, the drug should be stopped and the patient hospitalized. Dextrose by mouth or rectal drips in large amounts should be given, and from 5 to 10 units of insulin, three times daily ordered. If the symptoms are at all severe, intravenous injections of dextrose in large amounts should be given slowly as well. Proteins in the diet should be reduced to minimal amounts, as the liver is no longer fully capable of detoxicating the products of protein metabolism. Adler, according to Weigeldt,[43] advises the use of a combination of lactic acid, saline solution, dextrose and insulin together intravenously in the severest cases of liver atrophy, with the object of sparring for time until the necessary regeneration of the liver tissue occurs. As a last resort, Petermann of Berlin advises surgical drainage of the hepatic or common bile ducts. I have employed duodenal instillations of magnesium sulphate solutions, together with high carbohydrate diet and insulin injections.

41. Taubmann, Gert: Arch. f. exper. Path. u. Pharmakol. **121**: 204 (March) 1927.
42. Schroeder, K.: Ugesk. f. læger **84**: 1141 (Sept. 7) 1922.
43. Weigeldt, W.: Klin. Wchnschr. **9**: 285 (Feb. 8) 1930.

CONCLUSIONS

1. Cinchophen preparations may produce liver damage of varying severity to fatality.
2. This danger cannot be avoided by small doses, intermittent use, large amounts of fluid or associated use of sodium bicarbonate.
3. Since cinchophen is not a specific for arthritis, gout, myositis, neuritis or allied states, indiscriminate use and counter prescribing is dangerous, and the drug or its congeners should not be used in cases difficult of careful control and observation.
4. All cinchophen preparations and congeners should have their content advertised and noted on the container in which they are dispensed.
5. Protein sensitization of the liver may be responsible for the subsequent production of the liver damage by cinchophen.
6. Research work is needed to determine the factors in the production of liver damage and to prevent this dangerous effect.

651 St. Marks Avenue.

ABSTRACT OF DISCUSSION

DR. TORALD SOLLMANN, Cleveland: Time does not permit more than a brief glimpse of the more scientific problems that are suggested by Dr. Rabinowitz's presentation: the attempt to protect the liver by carbohydrates, reinforced by insulin, sounds reasonable. Its actual efficiency, however, cannot be decided until it is possible to furnish controls and this will probably require animal experimentation. This in turn is difficult because of the capriciousness of the hepatitis.

A hint is furnished by the promptness and frequency of the hepatic reactions from the intravenous injection of di-iodo-atophan (Biloptin) for choleography. This may be in line with the suggestion of Dr. Rabinowitz, that hepatic disorders predispose to cinchophen hepatitis, and suggest the possibility of its experimental production by combination with subeffective doses of other hepatitic agents, such as carbon tetrachloride. If this is successful it will furnish the possibility of testing the treatments. It will give a means for attacking the mechanism of the hepatitis; this may enable us to avoid such reactions.

At present, we are very much at sea. The liver seems to go the even tenor of its way through a great variety of major disturbances of the organism but goes completely to pieces under circumstances which would be considered much less violent; particularly in response to a miscellaneous variety of poisons. It would be interesting to learn how this is correlated with chemical structure. The relation is probably not directly to the benzene nucleus, as was suggested in the speculation of Willcox; at least, the action has not been demonstrated for most of the benzene derivatives and is much more marked with some aliphatic compounds, such as chloroform, carbon tetrachloride, and with phosphorus. It is quite possible, however, that these various hepatites may differ in nature as well as in causation.

DR. PHILIP S. HENCH, Rochester, Minn.: In the past, one has felt fairly secure in giving alkalis and rather large amounts of water when using atophan or cinchophen, but apparently these measures are not sure safeguards. Four patients have been brought to the Mayo Clinic with acute yellow atrophy of the liver. These patients had taken cinchophen elsewhere, not in large amounts, for fairly short periods of time, and on physicians' prescriptions. Two had had associated treatment with alkalis. One had used oxyliodide, one had had oxyliodide and another product containing cinchophen. Two had felt safe in using only the so-called best brand of cinchophen. At least one other patient had toxic hepatitis but recovered. Our patients did not relate, after careful questioning, any past experience that would lead us to suspect that their livers had been injured earlier in life, nor at necropsy did the microscopic examination reveal any evidence of previous hepatic disease. Two years ago, Dr. E. V. Allen and I, in spite of ample evidence of minor disturbances and occasional serious results, nevertheless gained the impression, in view of the wide use of this drug, that minor

disturbances resulted in only a very small percentage of persons who use it and that but a fraction of 1 per cent die from its use. The review by Dr. Rabinowitz will stimulate the attempt to answer several questions. Why was the toxicity of cinchophen so long unreported? Has there been a change in manufacturing? Are certain products really less toxic than others? Are certain batches of the drug itself toxic, or do only certain patients illustrate altered catabolism? If continued use of cinchophen is to be advocated, these questions should be answered. Many patients have large tolerance. One patient whom I had under observation for fifteen and a half years had taken from 40 to 90 grains (2.5 to 6 Gm.) of cinchophen daily, with no apparent discomfort or disability. Two and a half years later, under the observation of Dr. Haden of Kansas City, he still insisted on taking cinchophen for his arthritis. Hence, his amazing tolerance has continued for a period of eighteen years, which almost equals the entire history of treatment by cinchophen.

DR. ALEXANDER LAMBERT, New York: The peculiarity of the acute yellow atrophy due to cinchophen is so striking when one sees a case that I feel constrained to report one that occurred in Bellevue about two years ago, in the ordinary practice of a medical ward. The patient came in, pale, but under the paleness there was an increasing jaundice. He reported that he had had rheumatism, meaning pain in some joint or somewhere, and that he had taken what was to him a well known rheumatic remedy, the Harrell "Rheumatism Cure," which had been given to him by a neighbor, which had done that neighbor a great deal of good. He had taken evidently large amounts because he had taken it for eighteen months or two years. His jaundice rapidly increased and his fever rapidly increased. He died of acute yellow atrophy in a few days. I wrote to the American Medical Association and found that this rheumatic remedy contained large amounts of cinchophen and it was one of those cinchophen acute yellow atrophies. The reason that I think acute yellow atrophy is much less often diagnosticated is that the beginning of acute yellow atrophy is not of the stormy type that physicians have been taught to expect and, further, that jaundice in the majority of cases is diagnosticated as acute catarrhal jaundice. I know that this diagnosis must be universally taught because in the Fourth Division of Bellevue our interns come from all over the country and the invariable diagnosis of a slight jaundice by all kinds of interns taught by all kinds of teachers for many years has been acute catarrhal jaundice, which is the last thing usually that happens to a jaundiced patient.

DR. L. G. ROWNTREE, Rochester, Minn.: I wish to ask one question. What are we going to do about it? I have seen these cases in Rochester, and have seen the patients die despite everything we could do. I saw the patient, referred to by Dr. Hench, who had then been taking cinchophen for thirteen years. He asked me at the time about its toxicity. I told him I knew of no one who had taken so much. He insisted on taking it, as he said that it was the only thing that gave him relief from pain. I am asking the question as to whether there is in existence any mechanism for having this problem properly investigated. It would seem to me the most likely thing would be to have it taken by the officers of this section to the House of Delegates for consideration. I believe it is a sufficiently important problem to the health of the people to merit thorough investigation.

DR. WILLIAM S. COLLENS, Brooklyn: Dr. Sollmann recommended a scientific investigation of Dr. Rabinowitz's suggestion in regard to therapy. I should like to state the results of some experiments which Dr. Murlin and I conducted at the University of Rochester about two years ago that have a definite bearing on the therapeutic value of dextrose and insulin. In some experimentally produced degenerative changes in the liver by means of ligation of the hepatic artery we studied the value of dextrose intravenously in these dogs, using the respiratory quotient as a criterion or an index of its utilization, and we found that dextrose was not at any time utilized unless insulin was given along with it. That fairly confirms scientifically we think the suggestion that Dr. Rabinowitz makes about the value of insulin when dextrose is administered even to nondiabetic subjects. We have since had occasion to carry on the same experiments in patients who had cholecystectomies performed and who also showed, on resection of wedge-shaped sections of the liver for histologic studies, definite hepatitic changes such as were reported some years ago by Dr. Evarts Graham of St. Louis. We found there again that the respiratory quotient determinations following intravenous dextrose did not show any rise unless insulin was administered. This fairly well proves the value of Dr. Rabinowitz's suggestion that insulin administered with intravenous dextrose has a protective effect on a liver which is definitely degenerated.

DR. M. A. RABINOWITZ, Brooklyn: In answer to Dr. Rowntree's question, I had omitted part of a paragraph of my paper on the treatment. Adler, according to Weitgeldt, advises the use of a combination of lactic acid, saline, dextrose and insulin together intravenously in the severest cases of liver atrophy, with the object of sparring for time until the necessary regeneration of liver tissue occurs. As there is no organ in the body that has such capacity for regeneration as the liver, sparring for time might make it possible to save the patient. As a last resort, Petermann of Berlin advises surgical drainage of the hepatic or common bile ducts. This does not appear to me from a medical point of view as a most rational procedure, but he does report good results in severe liver atrophies of other causation.

STUDIES IN INFANT NUTRITION

VI. LACTOSE AND A MALTOSE-DEXTRIN PREPARATION *

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The studies have been carried on for eight years. They fall into two groups, chemical and clinical. The chemical work was done under the supervision of Dr. Chi Che Wang with the technical assistance of Miss Agnes A. Wood. All cow's milk was boiled one minute. The babies were normal infants more than 2 weeks of age, kept in a separate nursery, with special nursing provided by the hospital administration and the training school. Thus the infants escaped most of the parenteral infections so prevalent in any infants' ward. Experiments were never carried on when the babies were losing weight or seemed sick in any way.

PURPOSE OF THE WORK

According to the early theories of Finkelstein and L. F. Meyer, a diet containing excessive carbohydrate in cow's milk favored the development of diarrhea and nutritional disturbance. The mechanism was simple. Bacteria normally present in the intestine fermented the carbohydrate into various products, among these being lower volatile fatty acids, such as acetic and formic. Irritation of the intestine by these acids resulted in diarrhea, which in turn led to a disturbance of nutrition.

These theories found universal acceptance. Surprisingly little scientific work was done to confirm them. Ten years ago I thought it would be a simple matter to subject the hypothesis to chemical proof. One could prescribe a diet low in carbohydrate and determine the acids in the stool. Then the carbohydrate could be increased and the acids again determined. Unquestionably the increased carbohydrate would lead to increased intestinal fermentation and

* A summary of work done up to July, 1929. All routine urinalyses were done by one of our interns, Dr. M. L. Spivek.

* Read before the Section on Diseases of Children at the Eighty-First Annual Session of the American Medical Association, Detroit, June 27, 1930.

* From the Sarah Morris Hospital for Children, the Otto Baer Fund for Clinical Research and the Nelson Morris Institute for Medical Research of the Michael Reese Hospital.

increased acid output. The whole theory would then become a fact. The ideal carbohydrate for such experiments would, of course, be lactose.

LACTOSE IN INFANT NUTRITION

Discovered in the seventeenth century, lactose remained unmolested for 200 years. Then it became the target of the pediatricians. Before Escherich,[1] in 1886, had started his pioneer work on intestinal fermentation, Jacobi [2] had voiced his fear of the sugar because of the ease with which it changed to the dangerous lactic acid. From that time, although it is the sugar found normally in breast milk, its reputation in artificial feeding sank lower and lower.

Early writers [3] were not so concerned with its fermentability as with the impurities it contained. This fear was voiced by Brush [4] at a meeting of this section held at Nashville, Tenn., in 1890. He wrote, "Something must be wrong with some types of lactose because one does not find it in the urine of the breast fed." He found it in the urine of three artificially fed children. The metabolic conception of nutritional disease developed long afterward. Better methods of isolating lactose, devised by Soxhlet in 1893, did away with this objection.

New dangers were ascribed to lactose by Finkelstein and Meyer,[5] in that it exerted a specific pyrogenic action on the body. Schlutz,[6] in 1912, confirmed these experiments when lactose was given with sodium chloride.

At present it is safe to state that lactose is feared by all pediatricians chiefly on account of the ease with which it ferments in the intestine. Every textbook contains the same statement (Escherich, Czerny-Keller, Langstein and Meyer, Finkelstein, Feer, Heubner, Brennemann, Holt, Grulee). Individual studies [7] have offered the same conclusions, that lactose may be used in a normal infant but only with extreme care. A few writers [8] speak an occasional kind word for the sugar but Morse and Talbot, who certainly are the most friendly, warn that it should never be used in amounts over 7 per cent.

Clinical experience plus uncritical acceptance of the teachings of Escherich seem to have influenced most opinions.

Up to the latest writings the question is still disputed. Barenberg and Abramson [9] in the clinic of Alfred Hess have been daring enough to report excellent clinical results with lactose in infants more than 3 months of age. On the other hand, Paffrath [10] gave children solutions of various sugars and found lactose alone was responsible for diarrhea. Marriott in his new book reiterates the warning that lactose "cannot be used with as great safety or fed in as large amounts as other carbohydrates."

The preponderance of evidence then suggests that if one wishes to study nutritional disturbance arising from intestinal fermentation and diarrhea, lactose should be the ideal carbohydrate to use.

CHEMICAL RESULTS

These studies,[11] so simple in their inception, have taken ten years and are still under way.

Charts of the entire chemical and clinical study have been displayed in the scientific exhibit.

Time permits the demonstration of only a few to show some of the high points of the work.

With the stools of normal breast-fed infants taken as a standard, studies have been made of the stools of clinically normal infants while on cow's milk feedings, as well as of the stools of diarrheal children, both on breast and on cow's milk.

The stools of infants fed on whole cow's milk, who are clinically normal and do not give a clinical picture

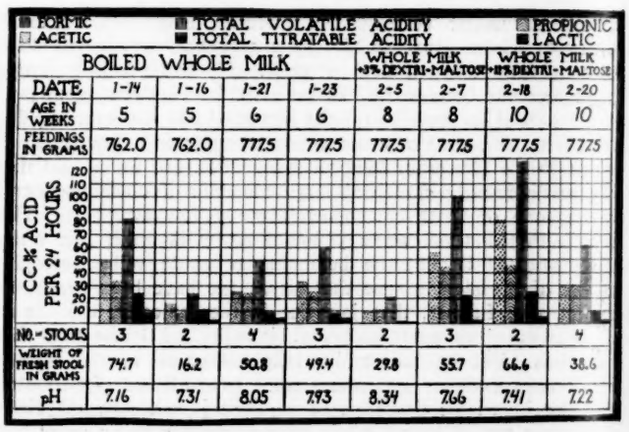
FORMIC
ACETIC
TOTAL VOLATILE ACIDITY
TOTAL TITRATABLE ACIDITY
PROPIONIC
LACTIC
BOILED WHOLE MILK
WHOLE MILK +3% DEXTRI-MALTOSE
WHOLE MILK +12% DEXTRI-MALTOSE
DATE 1-14 1-16 1-21 1-23 2-5 2-7 2-18 2-20
AGE IN WEEKS 5 5 6 6 8 8 10 10
FEEDINGS IN GRAMS 762.0 762.0 777.5 777.5 777.5 777.5 777.5 777.5
CC. N/10 ACID PER 24 HOURS
NO. STOOLS 3 2 4 3 2 3 2 4
WEIGHT OF FRESH STOOL IN GRAMS 74.7 16.2 50.8 49.4 29.8 55.7 66.6 38.6
pH 7.16 7.31 8.05 7.93 8.34 7.66 7.41 7.22

Chart 1.—The influence of the addition of 3 and of 12 per cent of the maltose-dextrin preparation to whole boiled cow's milk on the quantity of feces, the frequency of defecation, the excretion of total volatile acids and their salts, on total titratable, lactic acids and lactates, and on the hydrogen ion concentration, in a normal infant.

of diarrhea, compare as follows with those of normal breast-fed babies:

The stools of artificially fed babies are of greater weight for the twenty-four hour period. There is a somewhat greater output of lower volatile fatty acids and their salts, with a somewhat lowered output of lactic acid and lactates. The free acid, as shown by the total titratable acidity of the twenty-four hour specimen, is lower. The p_H (which represents "true" acidity) is considerably higher than that of the stools of the breast fed. Infants fed on cow's milk often pass nearly neutral or even slightly alkaline stools.

When infants fed on breast milk develop the clinical picture of diarrhea, they show an increased frequency of stools, with a small increase in their weight. The excretion of volatile fatty acids and their salts is slightly increased, as is also the excretion of lactic acid and lactates. The twenty-four hour figure for "total"

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titratable acidity is also increased. There is very little change in the p_H, which is the measure of the "true" acidity.

The stools of infants fed on cow's milk who develop diarrhea show a markedly contrasting picture. There is a great increase in weight of the stools, and a correspondingly great output of volatile acids and their salts, as well as of lactic acid and lactates. The figure for "total" titratable acidity is increased; however, the p_H remains toward the alkaline side, just as it does in normal babies fed on cow's milk. The older clinicians, considering figures for "total" titratable acidity, believed the stools of diarrheal children to be "very acid"; p_H measurements (which give "true acidity" as judged by the hydrogen iron concentration) show this concept to have been erroneous. The stools of infants fed on cow's milk are less acid than those of breast fed infants, whether they are diarrheal or not.

As cow's milk contains only 4 per cent lactose and breast milk 7 per cent, factors other than the *amount* of lactose in the diet determine how much of this lactose shall ferment. Unquestionably the problem becomes one of factors influencing lactose *absorption*.

What changes take place when lactose is added to whole cow's milk?

In a typical case the addition of 3 per cent lactose causes no great change in the picture of stool chemistry, except in hydrogen ion concentration. In infants with no diarrhea the addition of 3 per cent lactose increases the total titrable and lactic acids. Clinically the children seem much happier.

Changing to 12 per cent effects a noticeable chemical change but, to one's astonishment, exactly the antithesis of the one expected. The longer the child is on the mixture, the less is the quantity of acid excreted and the more do the stools resemble those of the breast

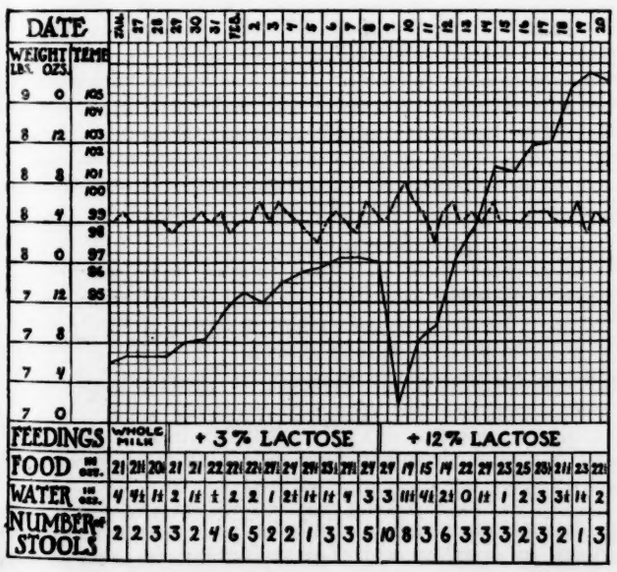

Chart 2.—This and chart 3 show that a diet of whole cow's milk with the addition of 3 per cent and later 12 per cent lactose continued over a number of weeks led to a severe loss of weight but with no diarrhea.

fed. Apparently the relation of lactose to protein, approximately 4 to 1, like that existing in breast milk, is most favorable to intestinal processes. In my desire to produce diarrhea experimentally by increasing the quantity of lactose in the diet, I was unconsciously bringing about a relation of lactose to protein which proved actually beneficial.

Chart 1 shows the effect of adding a preparation of maltose and dextrin [12] with 2 per cent sodium chloride to whole boiled cow's milk. It is introduced to show the slight effect that this carbohydrate exercises on the stool picture of whole cow's milk. In this chart the differential analysis for volatile acids can be disregarded.

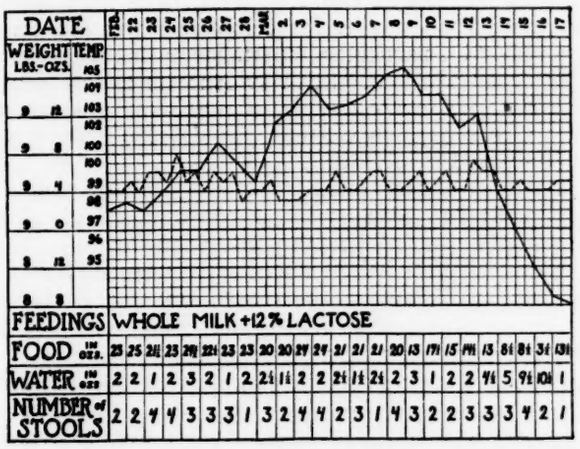

Chart 3.—This and chart 2 show that a diet of whole cow's milk with the addition of 3 per cent and later 12 per cent lactose continued over a number of weeks led to a severe loss of weight but with no diarrhea.

On whole cow's milk the stools are small, contain small amounts of free acid, little lactic acid and lactates, and show a hydrogen ion concentration toward the alkaline. Clinically the baby was constipated.

The addition of 3 per cent of the maltose-dextrin preparation causes little change except some increase in the total volatile acids and their salts.

To our surprise, the addition of 12 per cent of the maltose-dextrin preparation has almost no effect on the total free acid, lactic acid and lactates, stool weight and frequency, and hydrogen ion concentration, while there is a possible increase in the total volatile acids and their salts.

In this respect, the maltose-dextrin preparation is in striking contrast to lactose, and our analyses confirm its constipating alkalizing effect in the intestine.

LATER THEORIES

During the years that these experiments were being conducted, Finkelstein and Meyer modified their views. From clinical observation Finkelstein, in his book of 1921, believes that cow's milk causes a primary injury to the intermediary metabolism, and following such injury diarrhea develops as a secondary complication. Thus intestinal fermentation with resulting diarrhea becomes a result of disturbance of nutrition rather than a cause.

CLINICAL STUDIES

Our clinical studies favor the later hypothesis. After being convinced that lactose was not as dangerous as I had thought, and that in a well baby on a diet of whole cow's milk, a proper lactose-protein relationship improved diarrheal stools, I tried feeding a number of infants on whole cow's milk with 12 per cent carbohydrate.

Charts 2 and 3 show the clinical course of such a case. On whole cow's milk with 3 per cent lactose the infant thrived beautifully. A change to 12 per cent caused a temporary upset, but with no change of diet he recovered in twenty-four hours. Then for a

12. The preparation used was Mead's dextri-maltose.

period of weeks he became one of the show babies of the hospital. I thought I had discovered the real secret of infant feeding. One day with almost no warning he developed an alimentary intoxication. No parenteral infection could be demonstrated. The diagnosis was confirmed by a twenty-four hour tea diet with a resulting straightening of the weight curve. The critical loss of weight could scarcely have been due to decreased food intake, for complete starvation caused recovery. Of particular importance in this case was the *absence* of diarrhea. Such evidence is almost conclusive that the severest types of nutritional disturbance, even alimentary intoxication, can develop without gastro-intestinal involvement.

Chart 4 shows another striking clinical reaction. This baby had been on whole cow's milk with 12 per cent of the maltose-dextrin preparation for more than a month. Like the baby on lactose, he seemed in the best of health. Following the conclusion of the chemical experiments he was put on a diet of two-thirds cow's milk with 5 per cent of the maltose-dextrin preparation and discharged from the hospital. During the two weeks spent in trying to find a home for him he developed a mild otitis media. This infection, certainly not virulent clinically, precipitated the profoundest nutritional disturbance. Again the severest nutritional reaction is seen occurring without marked gastro-intestinal involvement. These studies certainly favor the Finkelstein hypothesis that injury to the general nutrition often precedes signs of intestinal fermentation.

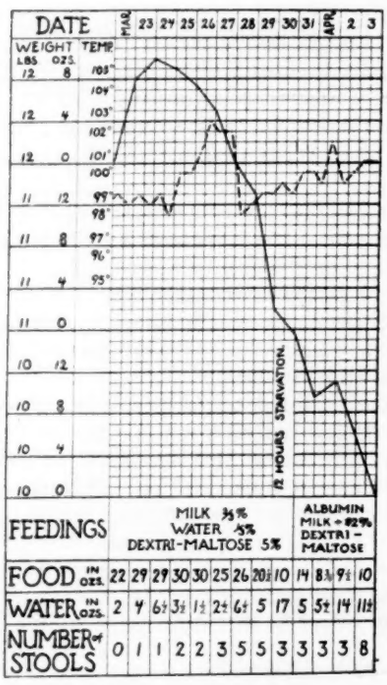
DATE
MAR 23 24 25 26 27 28 29 30 31 APR 2 3
WEIGHT LBS OZS
TEMP
12 8 103°
12 4 102°
12 0 101°
11 12 99°
11 8 98°
11 4 97°
11 0 96°
10 12 95°
10 8
10 4
10 0
12 HOURS STARVATION
FEEDINGS
MILK 3½% WATER 5% DEXTRI-MALTOSE 5%
ALBUMIN MILK + 2% DEXTRI-MALTOSE
FOOD IN OZS. 22 29 29 30 30 25 26 20½ 10 14 8¾ 9½ 10
WATER IN OZS. 2 4 6½ 3½ 1½ 2½ 6½ 5 17 5 5½ 14 11½
NUMBER OF STOOLS 0 1 1 2 2 3 5 5 3 3 3 3 8

Chart 4.—Alimentary intoxication induced by a very mild otitis media in an infant who had been on whole boiled cow's milk with 12 per cent of the maltose-dextrin preparation over a period of weeks. Diarrhea occurred only as a terminal complication.

COMMENT

The experiments are thus clearly divided into two groups.

Chemical studies have shown that lactose per se does not deserve its bad reputation. It can be given to a normal infant in good hygienic environment without undue risk, even with the additional digestive strain of whole cow's milk. If intestinal fermentation and diarrhea arise, they are not proportionate to the amount of lactose in the formula. Unquestionably some other element of cow's milk, probably by delaying lactose absorption, and thus permitting a greater total bacterial growth and increased fermentation, or by increasing peristalsis plays a great rôle. The relation of lactose to protein seems important. From studies previously reported,[11] parenteral infection plays the greatest rôle of all. Secondary in importance only to parenteral infection in influencing stool chemistry is the child's general nutrition.[11] The amount of lactose in the diet is not nearly as important as the factors which influence its absorption.

In regard to the maltose-dextrin preparation, the analyses of the stool showing low total and lactic acids and hydrogen ion concentration toward the alkaline confirm the clinical observations of its constipating tendency. Its value in true nutritional disturbance is not under discussion. When given to the normal infant in a mixture of cow's milk it results in changes in stool chemistry further from that of the breast fed than does lactose.

The second series of experiments, while offering clinical corroboration of some of the theories of nutritional disease, has raised a question which is still unanswered, which I doubt whether the experience of any one observer can answer. Whether the success of lactic acid milk is due to the lowering of the buffer as Marriott claims, or whether the fine curd is a factor as Brennemann recently suggested,[13] in either case the theory of the success of the mixture is in its digestibility. In our work whole cow's milk with carbohydrate seemed to effect a change in the infant's body predisposing to severe nutritional disturbance, and causing him to show the severest nutritional reaction following the mildest parenteral infection. These changes were independent of any gastro-intestinal disturbance. If normal stools can be taken as evidence, our mixtures were digested perfectly.

The addition of lactic acid to milk may make the mixture more digestible, but does it take away any of the factors which in our experiments seem to injure the body? It is significant that while pediatricians in this country discussed the effects of parenteral infections over fifteen years ago,[14] and in Germany long before that, no one fears them as does the St. Louis school. Is it possible that lactic acid milk plus high carbohydrate favors the development of nutritional disturbance following parenteral infection? This is just a thought which has occurred to me and I am putting it as a question. It is a question which cannot be solved except by the combined activities of all of us. The babies I studied were in a hospital. Perhaps if they had been at home with their mothers they would not have sickened on these diets. At any rate, I am bringing up the question in the hope of enlisting cooperation in seeking an answer.

It is interesting to reflect that in our ignorance we have blundered into efficient methods of milk modification. Empirically we keep an approximately favorable carbohydrate-protein ratio and in addition our milk dilutions prevent the dangers of overfeeding.

CONCLUSIONS

The conclusions can be divided into two groups:

A. Chemical studies show that:

1. Lactose added to whole boiled cow's milk does not result in diarrhea with a great increase in the excretion of acids when given to normal infants.

2. The amount of various acids excreted by the intestine does not depend directly on the amount of lactose in the diet but on various factors which are probably concerned in its absorption from the intestine. The relation of lactose to protein in the diet is of great importance.

13. Brennemann, Joseph: Curd and Buffer in Infant Feeding, J. A. M. A. **92**: 364 (Feb. 2) 1929.

14. Day, A. A.; and Gerstley, J. R.: A Study of Certain Cases of Infantile Diarrhea During the Summer of 1914, Am. J. Dis. Child. **9**: 233 (March) 1915. Gerstley, J. R.: Arch. Pediat. **33**: 671 (Sept.) 1916.

3. In respect to certain chemical relationships in the stool, lactose seems preferable to the maltose-dextrin preparation.

B. Clinical studies, dealing with the development of nutritional disturbance, favor the Finkelstein hypothesis that cow's milk causes a primary injury to the intermediary metabolism. Should intestinal fermentation and diarrhea develop, they are secondary and incidental to the primary disturbance of body nutrition. The severest nutritional disturbance may exist, even alimentary intoxication, without gastro-intestinal involvement.

ABSTRACT OF DISCUSSION

DR. F. W. SCHLUTZ, Chicago: The carefully conducted experiments of Dr. Gerstley go far to reestablish confidence in a food substance which for quite unaccountable reasons had fallen into considerable disrepute as a carbohydrate component for the infant's food. It is always difficult to reconcile this attitude with the fact that this particular sugar is native to human and all forms of animal milk that are used in infant feeding. I think Dr. Gerstley has quite conclusively shown that it is entirely safe even in large percentages and that its metabolism generally proceeds in a favorable manner. Whether this sugar is superior to other sugars is not quite clearly brought out and will, I believe, need quite a little further experimental evidence. Dr. Gerstley's work is interesting from another point of view in that it furnishes experimental data in confirmation of recent clinical experience, that high sugar percentages in the infant's food are not dangerous but may even have the reverse effect from the one that was generally expected and formerly predicted. The pediatrician today seems to have passed from the era of low sugar feeding to one of high sugar feeding. All this has given a changing concept of the mechanism and the factors which probably underlie, and are largely responsible, for the development of the dangerous diarrheal state. Dr. Gerstley pointed out some of these factors and suggested the thought and expressed the opinion which many have that, in the development of the dangerous state of alimentary intoxication, the carbohydrate component of the diet is only quite indirectly concerned. The picture of severe intoxication without the development of diarrhea which he showed in some of his charts is one with which many are familiar. I believe that studies of the kind Dr. Gerstley has made are greatly needed in the pediatrics and medicine of today. I think they will go far to replace theory by fact and feel that they will help in the finding of reasonable explanations for what in the past were so commonly empiric procedures.

Biologic Basis of Human Nature.—It is known that each of the thousand genes is a distinctive substance, having a definite function, a particular work to do in producing the new individual; so that if any one of them is destroyed or changed, development is altered in a definite way, and the resulting individual shows a corresponding change in his characteristics: a change perhaps in the color of his eyes, the shape of his nose, his stature; or in his temper or temperament. It is known that each different kind of a gene has its regular and invariable place in the string. Thus the different genes can be named or numbered, and a particular one is always the same gene, with the same rôle to play, and found at the same place in the chromosomes. . . . Each of our parents gives us a complete set of genes, strung up in the way we have described. So we have in every cell two such strings of genes, each one complete in itself. We are therefore double with respect to our genes. Each of the two sets in a cell contains all the materials that are necessary for producing an individual; a fact that has strange consequences. The mother gives us all the materials required for producing an individual of a certain type; the father also gives us the materials for producing another individual of another type. So we start life as double individuals.—Jennings, H. S.: The Biological Basis of Human Nature, New York, W. W. Norton & Co., Inc., 1930.

STUDIES ON DIGITALIS IN AMBULATORY CARDIAC PATIENTS

IV. NEWER PRINCIPLES OF DIGITALIS DOSAGE *

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AND
ARTHUR C. DeGRAFF, M.D.
NEW YORK

The practice of William Withering,[1] who published the first detailed study of digitalis about 150 years ago, is a matter not only of historical interest but of great practical importance to one dealing with the subject of digitalis dosage. At first glance it may appear as a stroke of genius that a fundamental law regarding the dosage of digitalis was stated at a time when practically nothing was known about the drug, not even that its beneficial effects were related to an action on the circulation. On the other hand, it may be the very fact that there were no distractions in the form of theories of cumulation and excretion or formulas of dosage that made it possible to keep the object clearly in view and to arrive at sound and practical principles. Physicians who profess to use a recommended plan of digitalis dosage frequently find their patients suffering from either insufficient or excessive digitalization. A common difficulty is illustrated by the following example: A physician recently made inquiry because, after having given a patient of a certain weight a daily dose of 4½ grains (0.3 Gm.) of digitalis for about three weeks, he found himself uncertain as to the next procedure when at the end of that time only moderate improvement had occurred and no toxic symptoms had resulted, although the total quantity had exceeded the dosage determined by an accepted method of calculation (Eggleston) and allowance was made for supposed daily excretion (Pardee). Withering's advice in such matters will bear frequent repetition: "Let the medicine be given until it either acts on the kidneys, the stomach, the pulse or the bowels; let it be stopped upon the first appearance of any of these effects." Expressed in modern phraseology, his recommendation was to give digitalis in dosage sufficient to produce the desired therapeutic results and to discontinue it when these are obtained or when minor toxic symptoms occur. In his monograph it is apparent that his practice was to give large doses at first and then to continue the treatment with smaller ones.

In the period of rationalization that followed this work, a great deal of knowledge was gained about the action of digitalis, but much confusion was also introduced by the substitution of *a priori* reasoning for painstaking clinical observations. Theories of cumulation instilled a fear of the drug that resulted in the use of such small quantities as 2 minims (0.12 cc.) of the tincture of digitalis three times daily. In a lecture before the Harvey Society in 1910, Cushny [2] deplored the common use of such inadequate dosage and stated that "The best results are obtained only by the largest doses which can be given without gastric or intestinal symptoms" and recommended doses of from 1 to 1½

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* Read before the Section on Pharmacology and Therapeutics at the Eighty-First Annual Session of the American Medical Association, Detroit, June 25, 1930.

* From the Third Medical Division (New York University) and Adult Cardiac Clinic of Bellevue Hospital, and the Department of Pharmacology of Cornell University Medical College.

1. Withering, William: An Account of the Foxglove, and Some of Its Medicinal Uses with Practical Remarks on Dropsy and Other Diseases, Birmingham, 1785.

2. Cushny, A. R.: The Therapeutics of Digitalis and Its Allies, Harvey Lectures, 1910-1911, p. 46.

drachms (4 to 6 cc.) of the tincture of digitalis daily. Eggleston,[3] in 1915, established the fact that even larger doses of digitalis may be given on the first day with a fair degree of safety, and frequently with great advantage under certain conditions, so that the full effects may be induced as early as eighteen hours after the oral administration of the dose. In 1922 Pardee,[4] in a paper dealing with the prolonged use of digitalis, expressed a view similar to Cushny's. He said: "We want as strong an action as the drug can exert, and so we try to continue the most effective degree of digitalization which is just short of poisoning." He advised that patients should first be brought to the point of saturation (to early toxic symptoms), should then, after an interval of a day or two, receive an average daily dose of 2 grains (0.13 Gm.) because he believed that the average patient excretes about 2 grains daily, and that that daily excretion dose "can and must be given in order to maintain the digitalis effect."

In the reaction to the use of very small doses of digitalis, practice has exceeded the limits recommended by Withering. An altogether too simple view of the matter has been commonly accepted; namely, that in order to produce the best results, it is necessary to digitalize all patients to a point just short of minor toxic symptoms, and that in order to maintain these results it is necessary to maintain the same "effective concentration" of the drug in the body. In the present communication we shall relate how it came to be suspected that these views regarding digitalis dosage are wholly inadequate to explain the response to the drug of the large proportion of ambulatory cardiac patients and to set forth evidence that supports the following conclusions:

1. In the average ambulatory cardiac patient there is a wide margin between the amount of the drug necessary to produce full therapeutic effects and the maximum amount that can be tolerated without toxic symptoms.

2. The "effective concentration" of the drug within the body necessary to maintain full therapeutic results is usually much lower than that necessary to produce them in the beginning.

3. The average ambulatory cardiac patient with auricular fibrillation can be satisfactorily digitalized by the daily repetition of a relatively small dose of the drug, which can then be continued for months or years as the daily maintenance dose without producing toxic symptoms.

4. The degree of heart failure determines the "effective concentration" of digitalis in the body necessary to produce full therapeutic effects and the average ambulatory patient with symptoms of heart failure requires a much lower "effective concentration" of the drug to attain this result than the average bedridden patient with far advanced congestive failure.

CUMULATION, A SELF-LIMITING PROCESS

It is well known that if the average cardiac patient were to receive a daily dose of 9 grains (0.6 Gm.) of an active specimen of digitalis, there would result a progressive increase in the intensity of digitalis action that would continue until toxic symptoms appeared. This is usually interpreted as signifying that the daily dose of 9 grains is more than the patient can excrete in a day, so that the drug continues to accumulate until a quantity is present sufficient to produce toxic symptoms. In a previous article we [5] called attention to the fact that when smaller doses of digitalis are repeated daily it can be shown that cumulation is a self-limiting process; that a suitable daily dose may give evidence of cumulation at first, and that then a level is reached, the effects showing no further increase in intensity even though the same daily dose continues to be administered. The behavior of a typical case is shown [6] in chart 1.

This patient had auricular fibrillation and had been in bed with an attack of congestive heart failure. When he appeared at the clinic he had been without digitalis for a period of three weeks. The ventricular rate was 122 a minute and there were moderate symptoms of cardiac failure. He was given a daily dose of 3 grains (0.2 Gm.), which produced progressive slowing of the ventricular rate and improvement in the symptoms of failure. After two weeks the condition reached a level which was then maintained by the same daily dose without interruption during the succeeding period of forty-two weeks in which he was observed.

The level of effect reached in these cases may be considered as representing a quantity of digitalis which has accumulated [7] in the body and which shows no appreciable variations as long as the same daily dose is continued.[8] The size of the daily dose determines the point at which cumulation ceases (equilibrium between the daily dose and daily excretion). Thus, while a daily dose of 3 grains (0.2 Gm.) in a given patient may lower the ventricular rate from 140 to 80 a minute and keep it at 80, a daily dose of 2 grains (0.13 Gm.) may only lower the rate from 140 to 110 and keep it at that rate, or a daily dose of 6 grains (0.4 Gm.) may lower it from 140 to 50 a minute and keep the rate at this new level with continued administration of the drug. In order to simplify the discussion we shall refer throughout this paper to the amount of digitalis effective when a given level is reached as the "effective concentration" of the drug within the body.

MARGIN BETWEEN MINIMUM DOSAGE FOR FULL THERAPEUTIC EFFECTS AND MAXIMUM DOSAGE TOLERATED WITHOUT TOXIC SYMPTOMS

Several years ago we began to make observations in the Adult Cardiac Clinic of Bellevue Hospital on patients with auricular fibrillation with the view of determining the average daily dose of digitalis necessary to maintain the full therapeutic effects that had been induced while the patient was in the hospital, and to ascertain to what extent that dose would vary with preparations of different potency. During this period approximately 800 ambulatory cardiac patients with auricular fibrillation were treated. Many of them were working. They all showed varying degrees of deficiency in cardiac reserve and with few exceptions had received hospital treatment for one or more attacks of congestive heart failure. When these patients were discharged from the wards of the hospital and enrolled in the clinic, the usual procedure was to begin with a dose of 2 or 3 grains daily. The drug was dispensed in the form of compressed tablets of the dried digitalis leaf and the daily quantity was directed to be

3. Eggleston, Cary: Digitalis Dosage, Arch. Int. Med. **16**: 1 (July) 1915.

4. Pardee, H. E. B.: The Continued Use of Digitalis, New York State J. Med. **22**: 131 (March) 1922.

5. Gold, Harry; and DeGraff, A. C.: Studies on Digitalis in Ambulatory Cardiac Patients: II. The Elimination of Digitalis in Man, J. Clin. Investigation **6**: 613 (Feb.) 1929.

6. In all the illustrative cases in this paper, digitalis leaf (specimen F) was used with a potency of 100 mg. per cat unit.

7. It is probable that cumulation is in part due to summation of effects in patients with heart failure.

8. It is possible that some changes may result from the gradual cumulation of slowly excreted fractions of the drug while rapidly eliminated fractions do not cumulate to the same degree.

taken in a single dose.[9] The patients were examined at intervals of one week or less frequently, depending on a number of circumstances. If toxic symptoms resulted, the daily dose was diminished. The average ambulatory cardiac patient with auricular fibrillation constantly suffers with some symptoms due to deficient cardiac reserve; hence, when the initial dosage produced no symptoms, it was usually increased in an effort to obtain further improvement, and the only way to learn whether greater therapeutic effects were possible in a given patient was to increase the size of the daily dose gradually to the point of minor symptoms. When these occurred the dose was again diminished and the largest amount that produced no toxic symptoms was then continued as the daily maintenance dose. We had previously followed the accepted idea that it was necessary to administer digitalis in the largest doses that could be tolerated without toxic symptoms. At first the study embraced only those patients who attended the clinic regularly and took the daily dose with few or no interruptions.

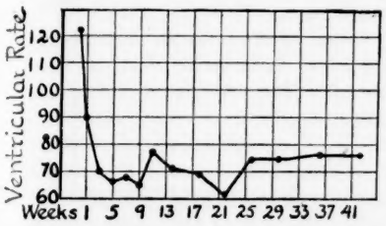

Chart 1.—Ventricular rate in patient E. Q., aged 25, weight 154 pounds (70 Kg.), with rheumatic heart disease, mitral stenosis and insufficiency, enlarged heart and auricular fibrillation; class II-a. The patient had had no digitalis for three weeks; class II-b. Three grains (0.2 Gm.) of specimen F was administered daily.

The first specimen of digitalis (specimen A) had a potency of 75 mg. per cat unit and was used for a period of about one and one-half years by the foregoing technic. It was then discontinued and a second specimen of digitalis (specimen C) was substituted and continued for about the same length of time. The potency of the second specimen was 140 mg. per cat unit. The initial trial doses of this specimen were usually the same in terms of grains as the final daily dosage of the first specimen, although the first was nearly twice as active as the second by the cat method of assay.

That specimen A was also much more active in man than specimen C was evident from the fact that some of the patients in the clinic showed signs of insufficient digitalization when the weaker preparation was substituted for the stronger one in the same grain dosage.[10] It was further confirmed by tests made on patients with congestive heart failure in the wards to whom 0.15 cat unit per pound of body weight of each preparation was given in a single dose. To some of these patients the stronger preparation was given first and, after an interval sufficient for the excretion of the drug, the weaker preparation was given in almost twice the quantity with practically identical results.

Two facts soon became apparent: First, while some of those patients who had been eliminated from the original study because they took digitalis irregularly suffered more marked symptoms of failure or gave objective evidence of inadequate use of the drug, it was rather striking that others showed no signs of insufficient digitalization. Second, the general condition of most of the patients was practically the same with identical doses in grains of the two preparations. As already stated, there were some exceptions in which larger doses of the weaker preparation had to be given to maintain the previous state of improvement.

An analysis was then made of a group of forty-six patients who had received the stronger preparation. The results showed the average daily dose to be $2\frac{3}{10}$ grains (0.15 Gm.). A similar analysis was made of a group of forty-two patients who received the preparation that was one-half as active. The results showed the average daily dose to be $2\frac{8}{10}$ grains (0.18 Gm.). With only few exceptions the two groups included the same patients and no patient was included who had not received each of the two specimens of digitalis for at least three months. It was also proved that these patients required digitalis because symptoms of failure appeared when the drug was withheld.

The foregoing facts therefore indicate that the average ambulatory patient with auricular fibrillation in whom improvement was maintained for long periods of time by what was approximately the maximum tolerated dosage was receiving much more digitalis than was necessary though no toxic symptoms were induced, and that much smaller doses sufficed to produce equally satisfactory therapeutic results.

This conclusion was tested in a somewhat different way in a number of cases in which the same specimen of the drug was employed in varying doses in the same patients. The results obtained in one case have been charted and serve as an illustration (chart 2). This patient had auricular fibrillation with moderate symptoms of congestive heart failure and a ventricular rate of 140 a minute. He had been without digitalis for a period of more than three weeks when he came under observation. After a daily dose of 3 grains (0.2 Gm.) for fourteen days the ventricular rate decreased to 81 a minute and all symptoms of failure disappeared. The continued use of this dose maintained this improvement. An increase of the dose by 100 per cent to 6 grains (0.4 Gm.) daily, produced no perceptible change in the condition. A further increase to 9 grains (0.6 Gm.) daily for seven days lowered the heart rate to 68 a minute, though the symptoms and signs remained the same. Thus the clinical condition during the period when the dose of 6 grains was taken was indistinguishable from that in which the one of 3 grains was used. This again illustrates the wide margin between the maximum tolerated dosage and that which is sufficient to produce or maintain the full therapeutic results in this class of patient.

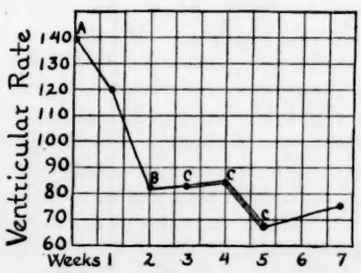

Chart 2.—Ventricular rate in patient J. H., aged 51, with rheumatic heart disease, mitral stenosis and insufficiency, enlarged heart and auricular fibrillation; class II-a. *A*, failure; *B*, marked improvement; *C*, same; the single line indicates 3 grains (0.2 Gm.) daily; double line, 6 grains (0.4 Gm.); three lines, 9 grains (0.6 Gm.).

In this chart, as in all the subsequent ones, only the ventricular rate is recorded as evidence of the intensity of digitalis action because it is a criterion that lends itself most satisfactorily to graphic presentation. The apex rate was counted by the stethoscope under fairly uniform conditions with the patient sitting or lying after a rest of several minutes. In most instances, other evidence of failure disappeared with the slowing

9. Gold, Harry; and DeGraff, A. C.: Studies on Digitalis in Ambulatory Cardiac Patients: I. The Use of Digitalis in the Cardiac Clinic, J. A. M. A. **90:** 1016 (March 31) 1928.

10. In these cases the dosage of specimen A may have been less than the maximum tolerated dose, or they may have been cases in which the latter is necessary to maintain the effects.

of the heart rate. We have gathered data bearing on the relative importance of the various criteria for estimating the intensity of digitalis action in patients with auricular fibrillation and these will be analyzed in a subsequent communication. It is well to state here, however, that while the ventricular rate is a very satisfactory index of digitalis action in most cases of auricular fibrillation there are many cases in which the intensity of action is not revealed in changes of the ventricular rate alone. It is not infrequently observed

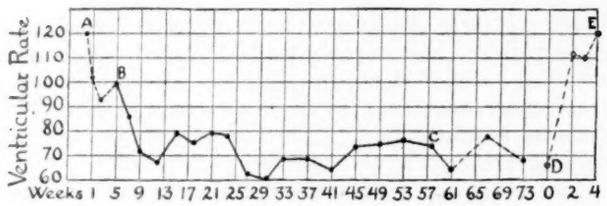

Chart 3.—Ventricular rate in patient T. K., aged 30, with heart disease of unknown origin, mitral stenosis and insufficiency, enlarged heart and auricular fibrillation; class II-a. *A*, failure, class II-b, 3 grains (0.2 Gm.) of specimen F daily; *B*, 4½ grains (0.3 Gm.) daily; *C*, 3 grains; *D*, digitalis discontinued; *E*, failure; class II-b.

that a given dosage lowers the heart rate to normal levels with only moderate improvement in the symptoms of failure, and with more intense digitalization the latter improve markedly though little or no further change in the heart rate occurs. On the other hand (with due caution against possible errors in interpretation), improvement in the subjective symptoms of failure is occasionally seen after doses of digitalis that have produced little or no slowing of a rapid ventricular rate.

"EFFECTIVE CONCENTRATION" OF DIGITALIS FOR PRODUCING FULL THERAPEUTIC EFFECTS VERSUS "EFFECTIVE CONCENTRATION" NECESSARY FOR MAINTENANCE

In order to induce the full effects of digitalis without undue delay it is necessary to give relatively large doses for the first few days, and since these doses, if continued, will induce toxic symptoms, the treatment is continued with smaller daily doses. This is a generally approved practice. It is commonly held, however, that these smaller doses should be equal to the amount of digitalis the patient excretes daily after full digitalization, in order to maintain the high "effective concentration" of the drug in the body induced by the larger doses. The very fact that most ambulatory patients after having been fully digitalized in the hospital were getting along satisfactorily with nearly one-half as much digitalis as they could tolerate without toxic symptoms is in itself an indication that such an "effective concentration" as is often necessary to induce effects is frequently unnecessary in order to maintain them. A number of observations bearing directly on this question have been made and the results in a typical case are reproduced in chart 3. The observations on this patient covered a continuous period of seventy-three weeks for this study. The patient had auricular fibrillation and had been attending the cardiac clinic for more than five years. When receiving adequate doses of digitalis he usually presented only slight evidence of deficient cardiac reserve. At the end of the chart there is a record of the changes occurring when the drug was withheld after a daily dosage of 4 grains (0.26 Gm.) for some time. Within two weeks the ventricular rate became rapid and after four weeks marked symptoms of failure appeared. It is evident, then, that for this patient the more or less continuous use of the drug was essential. At another period he had received a daily dose of 1½ grains (0.1 Gm.) for several weeks. This dose was inadequate and he gradually passed into congestive heart failure with a ventricular rate of 120 a minute, as seen at the beginning of the chart. It now became necessary to digitalize the patient again. A daily dose of 3 grains (0.2 Gm.) for one week resulted in only moderate improvement and slowing of the heart rate to about 100 a minute, and the continuation of that dose for four more weeks simply maintained that level. The dose was then increased to 4½ grains (0.3 Gm.) daily with the result that the rate returned to a normal range and all symptoms of failure disappeared. This dose was then continued daily for a period of fifty-three weeks without giving any evidence of greater digitalis action. It was then diminished to 3 grains (0.2 Gm.) daily, which now served to maintain the state of improvement during the subsequent period of observation of nearly four months. Thus, it is shown that, contrary to the common belief, a lower "effective concentration" of digitalis within the body may suffice to maintain the full effects than may be required to produce them in the beginning; and, as has already been shown, that the daily dose necessary to maintain these effects may be much smaller than that which can be excreted daily.

DIGITALIZATION BY A SMALL DOSE METHOD

In previous articles we [11] called attention to the fact that ambulatory cardiac patients with auricular fibrillation showing a rapid ventricular rate and varying degrees of heart failure, who have never received digitalis or in whom it was withheld for sufficiently long periods of time to allow for elimination of the drug, can be effectively digitalized by the daily repetition of a dose which may then be continued daily for long periods of time (months or years) without producing toxic symptoms. The daily doses ranged from 2 to 6 grains (0.13 to 0.4 Gm.), being occasionally as high as 9 grains (0.6 Gm.), and varied with different patients and with differences in potency of the drug. The records of thirty-four satisfactory courses of digitalization in twenty-one patients were published and, since

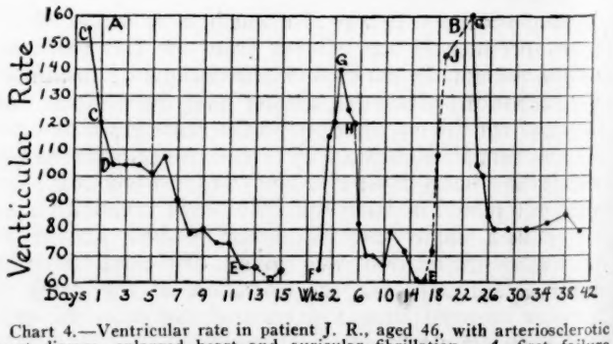

Chart 4.—Ventricular rate in patient J. R., aged 46, with arteriosclerotic heart disease, enlarged heart and auricular fibrillation. *A*, first failure (in hospital); functional class III; *B*, second failure (in clinic); functional class II-b; *C*, 24 grains (1.5 Gm.); *D*, 12 grains (0.8 Gm.) daily; *E*, digitalis discontinued; *F*, 3 grains (0.2 Gm.) daily; *G*, 6 grains (0.4 Gm.) daily; *H*, 9 grains (0.6 Gm.) daily; *J*, 4½ grains (0.3 Gm.) daily.

then, nine additional patients were proved [12] to have been fully digitalized [13] in that way. The behavior of

11. Gold, Harry; and DeGraff, A. C.: (Footnote 5); Studies on Digitalis in Ambulatory Cardiac Patients: III. Digitalization by a Small Dose Method, J. A. M. A. **92**: 1421 (April 27) 1929.

12. It has always been necessary to continue an experiment for several months in order to be fairly certain that the dose selected would not cause toxic symptoms. Only a small percentage of experiments started could therefore be completed satisfactorily and without interruption.

13. In all cases suitable care was taken not to attribute to digitalis results that were due to changes in effort (footnote 5).

a typical case has already been shown in chart 1. It should be noted that the full therapeutic effects were induced by the same 3 grain (0.2 Gm.) daily dose that the patient was excreting daily during the long period of maintenance. If he had not been excreting it, toxic effects would have resulted from cumulation. This illustrates a departure from the view

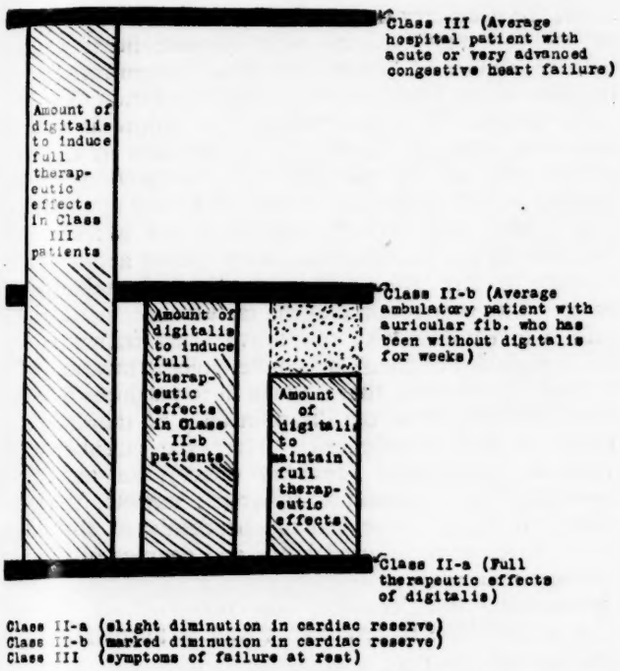
Class III (Average hospital patient with acute or very advanced congestive heart failure)
Amount of digitalis to induce full therapeutic effects in Class III patients
Class II-b (Average ambulatory patient with auricular fib. who has been without digitalis for weeks)
Amount of digitalis to induce full therapeutic effects in Class II-b patients
Amount of digitalis to maintain full therapeutic effects
Class II-a (Full therapeutic effects of digitalis)
Class II-a (slight diminution in cardiac reserve)
Class II-b (marked diminution in cardiac reserve)
Class III (symptoms of failure at rest)

Chart 5.—Dosage of digitalis that is necessary to produce full therapeutic effects varies with the degree of heart failure.

commonly held about the so-called daily excretion dose; the latter has been generally considered adequate to maintain effects produced by larger doses but not sufficient to produce them in the first place. In those papers we presented reasons for the belief that the foregoing phenomenon is explained by the fact that the amount of digitalis excreted daily is in all probability not a fixed quantity, and the dose that was excreted daily after some drug had accumulated in the body was not being completely excreted at the beginning.

DEGREE OF HEART FAILURE A FACTOR IN DOSAGE

While the larger proportion of ambulatory cardiac patients with auricular fibrillation can be successfully digitalized by the "effective concentration" of the drug reached by the daily repetition of relatively small doses, there is ample experience to show that such daily quantities are quite inadequate to induce full therapeutic effects in most patients with very advanced congestive heart failure. That the degree of heart failure is an important factor in determining the amount of digitalis necessary to produce full therapeutic results has been further tested in a number of observations, of which the following is an illustration (chart 4). This patient had auricular fibrillation and was admitted to the hospital in advanced congestive heart failure with a rapid ventricular rate. During a control period in bed for nineteen days the condition did not improve appreciably. He then received large daily doses of digitalis, 24 grains (1.55 Gm.) daily for the first two days, then 12 grains (0.78 Gm.) daily, with the result that marked improvement occurred, the ventricular rate slowed, the edema disappeared with a loss in body weight of about 30 pounds, or 13.6 Kg. (170 pounds to 140 pounds, 77 Kg. to 63.5 Kg.) and the patient was up and about after the sixth day. After his discharge from the hospital a daily dose of 3 grains (0.2 Gm.) for three weeks was insufficient to maintain the effects, and then a daily dose of 6 grains (0.4 Gm.) for two weeks was inadequate to restore the results obtained in the hospital. It was increased to 9 grains (0.6 Gm.) daily and this resulted in full digitalization, which was maintained for eleven weeks by the same daily dose. The drug was then withheld and at the end of five weeks moderate symptoms of failure and a very rapid ventricular rate developed. This time the daily administration of 6 grains (0.4 Gm.) of the same specimen of the drug was sufficient to produce full digitalization and to maintain the effects for a period of observation of sixteen weeks. In this patient, therefore, when failure began to reappear shortly after his discharge from the hospital as the result of an inadequate maintenance dose of digitalis, a daily dose of 6 grains (0.4 Gm.) was insufficient to check it appreciably. This dose, however, was quite sufficient to digitalize the patient satisfactorily in a mild attack of failure after a prolonged period of several months of improvement.

The conception that develops from these observations regarding the "effective concentration" of digitalis neccessary under different conditions is represented schematically in charts 5 and 6. It may be seen from chart 5[14] that patients with very advanced congestive heart failure require more digitalis to produce full therapeutic effects than those with symptoms of failure of lesser degree. A corollary of this fact is the further observation that the "effective concentration" necessary in order to produce the full effects is frequently much higher than is necessary in order to maintain them. These facts are illustrated from a somewhat different angle in chart 6. It shows that while there is a wide margin between the dose necessary

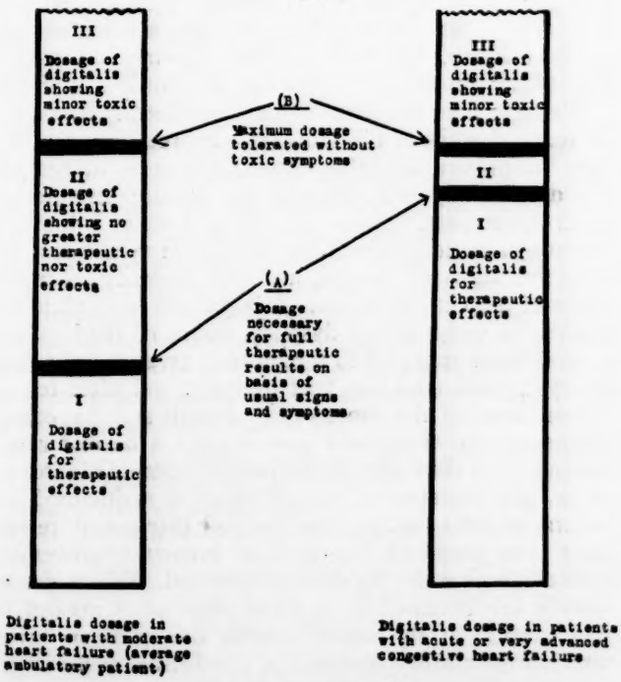
III
Dosage of digitalis showing minor toxic effects
II
Dosage of digitalis showing no greater therapeutic nor toxic effects
I
Dosage of digitalis for therapeutic effects
(B)
Maximum dosage tolerated without toxic symptoms
(A)
Dosage necessary for full therapeutic results on basis of usual signs and symptoms
III
Dosage of digitalis showing minor toxic effects
II
I
Dosage of digitalis for therapeutic effects
Digitalis dosage in patients with moderate heart failure (average ambulatory patient)
Digitalis dosage in patients with acute or very advanced congestive heart failure

Chart 6.—Margin between dosage necessary for full therapeutic results and maximum dosage that may be tolerated without toxic symptoms in patients with moderate and severe heart failure.

14. The functional classification in the illustration is based on the plan adopted by the Heart Committee of the New York Tuberculosis and Health Association.

for full therapeutic effects and that which produces toxic symptoms in patients with moderate symptoms of failure, this margin is often very small in patients with acute or very advanced congestive heart failure. In the latter, the margin is sometimes rendered even smaller by the greater susceptibility to some of the minor toxic symptoms, such as premature contractions. This is frequently seen in the terminal stages of heart disease.[15]

THE AMBULATORY CARDIAC PATIENT VERSUS THE BED PATIENT

For practical purposes it is well to consider two general groups of patients with auricular fibrillation presenting symptoms of heart failure. One is the type generally found in the wards of the hospital; the other is the ambulatory patient of the cardiac clinic. There is, of course, no sharp distinction between the two, and a given patient may at different times belong to one group or the other. The classification is employed to convey the idea of the distinction between patients with acute or far advanced heart failure showing marked symptoms at rest, and those that have more moderate symptoms, or symptoms only after exertion, who are able to be up and about, or may even be engaged in some light occupation. As already stated, it has been abundantly demonstrated that rapid digitalization with large doses frequently gives the best results in the very advanced degree of failure of the hospital patient. In this type the amount the patient needs is frequently the largest that can be tolerated without toxic symptoms. In the average ambulatory patient, however, such a high "effective concentration" is usually unnecessary. A much lower "effective concentration" produces equally satisfactory therapeutic results, though the higher one can be tolerated for years without showing any greater therapeutic results or producing any toxic symptoms.

We have used the term "equally satisfactory therapeutic results" while at the same time appreciating the fact that the present available criteria are quite inadequate for determining when results are equally satisfactory in every respect. There are at least three important factors to be considered: the subjective symptoms, the objective signs of failure, and the tendency to recurrence of attacks of failure. If a patient with auricular fibrillation with marked dyspnea, edema of the legs and a ventricular rate of 140 a minute is given a daily dose of 4½ grains (0.3 Gm.) of digitalis, and after ten or fifteen days all the shortness of breath and the edema disappear, the ventricular rate reaches a normal range around 75 or 80 a minute, the patient resumes his former work, and the state of improvement is maintained for several months, we say that the full therapeutic results have been produced, provided no greater improvement is in evidence when the dose is increased. When similar results are obtained by a daily dose of 3 instead of 4½ grains, in the same patient, the question arises whether the smaller dose will be as effective as the larger one in preventing the recurrence of heart failure in the course of years. There have been no systematic studies of this question and it is hardly necessary to state that such an investigation, though difficult to carry out, would yield information of great practical value. In the present state of knowledge it is more logical to follow the principle of digitalis dosage laid down by Withering, which is not to give as much digitalis as patients can tolerate without toxic symptoms, but only so much as is necessary to produce full therapeutic effects judged by the available criteria of improvement.

15. Gold, Harry; and Otto, H. L.: A Clinical Study of Digitalis Bigeminy, Am. Heart J. 1: 471 (April) 1926.

PRIMARY AND SECONDARY DIGITALIS EFFECTS

The phases of the problem of dosage for the production and maintenance of digitalis effects that have been discussed are, we believe, merely different aspects of the primary idea that the degree of heart failure determines the necessary dosage.[16] The probable explanation of the fact that patients with extreme heart failure usually require a higher "effective concentration" of digitalis in the body to restore the circulation than the same patients in a lesser degree of failure is closely bound up with the subject of the duration of digitalis effects and will be discussed in a forthcoming paper dealing with that subject. Suffice it to say at this time that neither differences in absorption nor excretion of the drug in the two states of heart failure appear to be factors of any great importance in the majority of cases. The production and the maintenance of digitalis effects in patients with congestive heart failure is not to be regarded as a case of simple biologic titration with a drug, in the sense that a given dose produces a given effect and that with the disappearance of the drug the effect at once disappears. After the circulation is restored by digitalis (primary effect), an important secondary factor becomes apparent; namely, the tendency to remain improved independently of the drug. This varies with different kinds and degrees of cardiac damage and in all probability plays a significant rôle in determining the "effective concentration" of digitalis that is necessary to produce as well as to maintain full therapeutic results.

There are wide variations in the amounts of digitalis recommended by different authorities. This is partly due to the fact that preparations of different potencies are employed, often affording no basis for comparing actual dosage. This subject is discussed in a recent paper by Wyckoff, Gold and Travell.[17] They also pointed out that differences in the potency of different preparations may sometimes escape detection in the wide margin between the minimum doses that produce the full effects and the maximum doses that can be tolerated without toxic symptoms. Another important source of confusion regarding dosage, however, is the fact that patients with symptoms of heart failure have been regarded in the past as a homogeneous group from the standpoint of their needs for the drug. At a time when very large doses were considered dangerous, patients with far advanced cardiac failure were inadequately treated, whereas at the present time, when digitalization to the point of minor toxic symptoms has come to be generally regarded as essential, the average ambulatory patient with mild symptoms of cardiac failure is receiving far more digitalis than is necessary.

SUMMARY

1. In the average ambulatory cardiac patient with auricular fibrillation and moderate heart failure a much lower "effective concentration" of digitalis in the body suffices to produce full therapeutic effects than is required in the average bedridden patient in advanced congestive failure.

2. We have shown that, in the ambulatory patient, full therapeutic effects, as judged by the usual clinical

16. Throughout this paper we refer to differences in effective dosage, i. e., after absorption has taken place and not to differences that might result from poor absorption.

17. Wyckoff, John; Gold, Harry; and Travell, Janet G.: The Importance of Differences in the Potency of Digitalis in Clinical Practice, Am. Heart J. 5: 401 (April) 1930.

criteria of improvement, can be produced by daily repetition of a relatively small dose of the drug that can then be continued as the daily maintenance dose without producing toxic symptoms. As is well known such results cannot be obtained with such small doses in the average patient with far advanced congestive failure; the larger daily doses usually required in these cases cannot be long continued without producing toxic symptoms.

3. In the average ambulatory cardiac patient there is a wide margin between the minimum dosage that produces full therapeutic results and the maximum that can be tolerated without toxic symptoms. This margin is frequently smaller in patients with far advanced failure and the latter often require the largest dosage that can be tolerated in order to produce the best results.

4. It is the accepted practice to use relatively larger doses of digitalis to produce the full therapeutic effects and then relatively smaller daily ones in order to maintain these results for long periods of time. The usual explanation is that the smaller doses are necessary in order to maintain the high "effective concentration" of the drug produced by the larger ones. Evidence has been set forth proving, however, that the "effective concentration" of the drug within the body necessary to maintain the full effects is usually much lower than that required to produce them in the beginning.

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THE THERAPEUTIC VALUE OF DIGITALIS IN PNEUMONIA *

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The work of Cohn and Jamieson [1] definitely established that there is a digitalis action on the heart in lobar pneumonia. In an address given in 1916 on the use of digitalis in pneumonia, Cohn [2] concluded that this drug did no harm and might be life saving. He suggested that it might be given to all patients as a routine, and explained the method of dosage in operation at the Hospital of the Rockefeller Institute. This extremely careful work and these conservative suggestions naturally influenced medical thought throughout the country, so that during the next ten years the routine giving of digitalis to patients with lobar pneumonia became a not uncommon procedure in many clinics, including Bellevue Hospital and most of the other large hospitals in New York.

However, during the period in which digitalis was given, no studies of comparative mortality were made between groups of patients with pneumonia receiving digitalis, and others from whom it was withheld. In Bellevue Hospital the study by the Columbia, Cornell and New York University Medical Divisions in the cases of lobar pneumonia with reference to specific antipneumococcus therapy by the control method provided a machinery that could readily be adjusted to include an investigation of the effects of the use or nonuse of digitalis as routine therapy in this disease as well. It seemed, therefore, an ideal time to investigate the action of the drug in cases of pneumonia, through the opportunity to use methods more favorable to constructive conclusions than had hitherto been employed.[3]

METHOD

In other studies of the value of digitalis in pneumonia there were none in which simultaneous observation under identical conditions were made on similarly selected groups of patients treated with digitalis and patients from whom digitalis was withheld. If sound conclusions are to be drawn, it is essential that both groups of patients, those receiving digitalis and those from whom digitalis is withheld, be selected similarly and simultaneously.

The analysis of hospital records of previous years with the study of digitalis untreated and treated groups does not constitute a properly controlled series. As a rule, under these circumstances, digitalis was not given in the milder cases of pneumonia, while it was thought necessary in the more severe cases and the patients were given it. This fact is well brought out by Randolph [4] in his analysis of 100 consecutive cases at the George Washington University Hospital, by Cohn and Jamieson [1] in their study of 105 cases at the Rockefeller Institute, and by Burrage and White [5] in their analysis of 221 cases during a five year period at the Massachusetts General Hospital. A further method of selection of controls, as done by Hart [6] in his study of influenzal pneumonia, in which a considerable number of controls "were selected at random from time to time," does not seem satisfactory. Nor yet does the comparison of untreated cases observed during one period of time with cases treated with digitalis during another period seem justified, as was done by Stone, Phillips and Bliss,[7] and later again by Stone,[8] since other methods of treatment as well as virulence of infection differ greatly from time to time.

In the present study it was decided that patients should be selected for the digitalis or nondigitalis groups in the following way: Patients were received into the "pneumonia series" according to the date and hour of admission, and alternate patients were treated with serum. The combination of serum and digitalis therapy led to the grouping of patients into four classes, selected only by the time of admission, and termed arbitrarily A, B, C and D. The treatment of the patients in these four classes was as follows:

Class A received neither serum nor digitalis.
Class B received serum only.
Class C received digitalis only.
Class D received both serum and digitalis.

This system of classification operated in each ward independent of other wards, so that factors of general care and nursing might be the same for each class of treatment.

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* Read before the Section on Pharmacology and Therapeutics at the Eighty-First Annual Session of the American Medical Association, Detroit, June 25, 1930.

* From the First (Columbia), Second (Cornell), and Third (New York University) Medical Divisions of Bellevue Hospital, and from the Departments of Medicine of Columbia, Cornell and New York University.

1. Cohn, A. E., and Jamieson, R. A.: The Action of Digitalis in Pneumonia, J. Exper. Med. **25**: 65-81 (Jan.) 1917.

2. Cohn, A. E.: The Use of Digitalis in Pneumonia, New York M. J. **105**: 234 (Feb.) 1917.

3. The committee for the study of digitalis in pneumonia is composed of Drs. Norrie and Woodruff of the First (Columbia University) Medical Division, Drs. Du Bois, Niles and Eggleston of the Second (Cornell University) Medical Division, and Drs. Wyckoff and DeGraff of the Third (New York University) Medical Division of Bellevue Hospital.

4. Randolph, B. M.: The Cardiovascular Problem in Pneumonia, Arch. Int. Med. **43**: 248-266 (Feb.) 1929.

5. Burrage, W. S., and White, P. D.: Digitalis in Pneumonia, Am. J. M. Sc. **174**: 260-264 (Aug.) 1927.

6. Hart, T. S.: The Heart in Bronchopneumonia: Observations on the Activity of the Heart and Its Response to Digitalis Made During the Recent Epidemic, Am. J. M. Sc. **158**: 649-658 (Nov.) 1919.

7. Stone, Willard; Phillips, B. J., and Bliss, W. P.: A Clinical Study of Pneumonia Based on 871 Cases, Arch. Int. Med. **22**: 409-439 (Oct.) 1918.

8. Stone, W. J.: The Heart Muscle Changes in Pneumonia with Remarks on Digitalis Therapy, Am. J. M. Sc. **163**: 659-668 (May) 1922.

Criteria of diagnosis were those ordinarily used to establish the diagnosis of lobar pneumonia; namely, typical history, physical observations, characteristic sputum, pneumococcus typing and fluoroscopic examination, verified whenever possible by postmortem examination. In the first year of the digitalis study (1927-1928), all cases of lobar pneumonia were included in the series regardless of the duration of the disease on admission or of general complications. In the second year (1928-1929), cases with history of onset more than eight days previous to admission or with general system disease were excluded from the digitalis-serum series; but of the cases thus excluded, any that showed evidence of cardiocirculatory disease were studied in the digitalis series as extra cases and were treated with or without digitalis according to the time of their admission, with reference to the regular A, B, C and D grouping.

In a large, active service such as that at Bellevue Hospital, it is difficult under ordinary circumstances to be certain that medications are always given exactly in the form and at the hour ordered, but in this special study every precaution was taken to know precisely how and when the digitalis was administered. The "digitalizing dose" for each patient was put in a small cardboard box labeled with the patient's name and given to the nurse in charge of the ward. The order for digitalis was written both in the ward and in the order book and on a manila tag fastened securely to the patient's bed. When the nurse gave the digitalis, she initialed the tag and wrote on it the exact hour of administration. These tags, later collected, constituted a permanent record.

Identical observations were made on patients who received digitalis and those from whom digitalis was withheld. The usual clinical and laboratory observations were taken, such as temperature, pulse, respirations and blood pressure, urinalysis and Wassermann reaction, and frequently morphologic and chemical examination of the blood. In addition, every patient was electrocardiographed daily during the febrile period, and every other day thereafter. A control tracing was taken on all digitalis-treated patients before any digitalis was administered. A total of 2,668 electrocardiograms were taken in the first year, and 3,369 in the second. Of the 835 patients studied in both years, 625 were electrocardiographed three or more times, 153 had one or two tracings, and 57, or less than one tenth, died before any tracings were taken at all.

A special staff was appointed to carry out the work along the method outlined. A full-time fellow was in resident charge of the work each year,[9] and was assisted by an electrocardiographic technician and a diener. This staff was working in addition to the staff then studying the serum treatment, and to the regular intern staff of the hospital.

DIGITALIS

Previous to the beginning of the investigation, different preparations of digitalis had been used in the three services. In the Columbia University service, the regular Bellevue Hospital preparation of digitalis was used. In the Cornell University Service, a preparation which we will call B was in use. This had been standardized by the manufacturer and was said to have a potency of 66 mg. equivalent to one cat unit by the cat unit method of Hatcher. In the New York University Division a preparation standardized by the manufacturer was in use which was said to have a potency of 100 mg. equivalent to one cat unit. These preparations had been in routine use in the wards and at this time there was no reason to doubt the reliability of the standardization. However, as it was desired to use a standardized preparation in all three services it was decided to discontinue the use of the unstandardized hospital digitalis in the Columbia Division and to use in its stead on this as well as in the Cornell Service preparation B, and to use in the New York University service a preparation which we will call A.

On its being noted that there was a high incidence of toxic signs for patients treated with the B preparation, it was found that this specimen of digitalis was approximately twice as active as the manufacturer had stated, in terms of cat unit potency. Reports dealing with the standardization of this preparation have been published.[10] When the error in standardization had been proved, a third noncommercial standardized preparation of digitalis was administered to patients in all divisions. This preparation, designated preparation G, had a potency of 100 mg. equivalent to one cat unit. While this occurrence resulted in unfortunately high dosage to a number of patients, it enabled us to study three groups: patients receiving too little dosage, optimum dosage (as far as could be determined) and high dosage.

DOSAGE

It was realized that in acute disease such as pneumonia, patients have to receive their digitalis rapidly. At the same time it was felt that the production of toxic effects should be prevented if possible. For this reason it was decided to give the digitalis in divided dosage, in no case giving a patient a digitalizing dose of more than the amount of 0.15 cat unit per pound of body weight, and to stop the administration of the drug on the appearance of any suggestive toxic symptom even though the full calculated amount had not been given. During the first year the dose was divided into parts approximating 30, 30, 15, 15 and 10 per cent of the estimated dose and these were given at intervals of six hours, the last dose (when given) being given about twenty-four hours after the first. As it was deemed unwise and unnecessary to weigh these patients, they were divided roughly into three groups, those who appeared to weigh less than 125 pounds (56.7 Kg.), those weighing between 125 and 175 pounds (79.4 Kg.) and those weighing over 175 pounds.

Because of the incidence of toxic signs, especially vomiting and the higher grades of heart block, in the digitalis-treated cases before the specimens were restandardized, it was decided, in the second year of the investigation, to reduce the dosage. Patients were then divided into two weight groups instead of three, those weighing above and below 150 pounds (68 Kg.). The lighter weight group received a total digitalizing dose of ten cat units, or 1 Gm., and the heavier 12.5 cat units, or 1.25 Gm. This was administered in three doses, the first 50 per cent of the total, the second 25 per cent, given twelve to eighteen hours after the first, and the third dose, 25 per cent, given after another interval of from six to eight hours. This dose compares closely with that given by Cohn and Jamieson.[1] They

9. The Fellows in Medicine in immediate charge of the digitalis investigation were J. Allen Yager, M.D., during the first year; Janet G. Travell, M.D., the second year and Margery Shearer, M.D., during the third year. The authors wish to express their appreciation for the invaluable services rendered by the Fellows.

10. Wyckoff, John; and Gold, Harry: A Dangerous Preparation of Digitalis, J. A. M. A. **94**: 626 (March 1) 1930. Wyckoff, John; Gold, Harry; and Travell, Janet G.: The Importance of Differences in the Potency of Digitalis in Clinical Practice, Am. Heart J. **5**: 401-411 (April) 1930.

had observed with 0.8 Gm. definite digitalis effects on the electrocardiogram in pneumonia, and their usual dosage [2] was between 1 and 2 Gm. Hart [6] also used a similar dosage in the treatment of influenzal pneumonia, giving 25 minims (1.5 cc.) of the tincture every four to six hours for six doses, or a total of the equivalent of 1 Gm. in twenty-four hours, and 24 minims daily thereafter, or the equivalent of 0.3 Gm. Stone [8] used a dosage of 4 cc. of tincture digitalis given every four hours for six doses, or a total dose the equivalent of 1.6 Gm. of powdered leaf in twenty-four hours, and no daily maintenance dose.

In our investigation, a daily maintenance dose of two cat units was given in both years. This was administered in a single dose each morning, and was discontinued when the temperature became normal or if toxic signs developed.

It was particularly difficult to determine proper dosage from the experience of others because most investigators either used no standardized preparation of digitalis, or, if a standardized preparation were used, the fact that it had been standardized was noted without estimation of its potency.

TABLE 1.—*Comparative Mortality of Digitalis Untreated and Treated Patients for the First and Second Years of the Investigation* *

	No Digitalis			Digitalis			
Year	Number of Patients	Number Died	Mortality, per Cent	Number of Patients	Number Died	Mortality, per Cent	Difference in Mortality
1.....	197	68	34.5	158	67	42.4	7.9
2.....	207	68	32.9	180	73	40.6	7.7
1 and 2.....	404	136	33.7	338	140	41.4	7.7

* In tables 1, 2, 3, 4 and 6, patients discharged at their own risk, patients in the C and D (digitalis treated) series who received no digitalis, and deaths within twenty-four hours after admission have been excluded.

In all, 834 cases were studied. A few of these patients were discharged from the hospital at their own risk on the request of responsible relatives; several others in the groups scheduled to receive digitalis, through error, received none. These, and all patients dying within twenty-four hours after admission, were excluded from the tabulations. There remained 742 patients.

Table 1 shows the gross results of the study. It must be remembered that a difference of 7.7 per cent in a mortality of 33.7 per cent means an increase in mortality of more than one fifth. The mortality of the digitalis group and the group receiving no digitalis is consistent for both years. This is particularly noteworthy because during the second year the dose was greatly reduced, as has been stated. A later study, however, shows that this high mortality occurs in patients getting the larger doses, even in the second year.

TABLE 2.—*Mortality of Males and Females for Digitalis Untreated and Treated Patients*

	No Digitalis			Digitalis			
Sex	Number of Patients	Number Died	Mortality, per Cent	Number of Patients	Number Died	Mortality, per Cent	Difference in Mortality
Male.....	357	123	34.5	299	125	41.8	7.3
Female.....	47	13	27.7	39	15	38.5	10.8

The sex distribution was preponderatingly male for the series, but table 2 shows that the sex ratio was consistent both in the group receiving digitalis and in that from which the drug was withheld. The female series is so small that it is doubtful whether the difference of 3.5 per cent greater mortality among the women receiving digitalis is of significance.

TABLE 3.—*Mortality of Age Groups for Digitalis Untreated and Treated Patients*

	No Digitalis			Digitalis			
Age Group in Years	Number of Patients	Number Died	Mortality, per Cent	Number of Patients	Number Died	Mortality, per Cent	Difference in Mortality
10 to 29	94	15	16.0	73	19	26.0	10.0
30 to 39	109	30	27.5	76	25	32.9	5.4
40 to 49	99	40	40.4	99	44	44.4	4.0
50 plus	102	51	50.0	90	52	57.8	7.8
Totals.....	404	136	33.7	338	140	41.4	7.7

Table 3 shows age distribution in the groups receiving and not receiving digitalis. The distribution is extremely consistent in the patients who did not take this medicine; in the group which did receive digitalis there are about 6 per cent more over the age of 40 than under. Brooks [11] advises routine digitalis therapy in older patients. In this series, digitalis did not reduce the mortality in the older age groups; the patients over 50 receiving digitalis showed a mortality of 7.8 per cent higher than patients in the same age group not receiving the drug.

It is known that the mortality in pneumonia is different in the various types. Patients with type I pneumonia have a relatively low mortality and those with type II a very large mortality. Table 4 compares the type incidence in the two groups. It is shown that it is consistent in both, and that the difference in mortality in the group receiving and not receiving digitalis cannot be due to a preponderance of a low mortality type such as type I or of a high mortality type such as type II occurring in one of the two groups. It shows that the mortality is always higher in the group receiving digitalis except for type II; patients in type II receiving digitalis actually had a mortality of 2.3 per cent lower than patients not receiving it.

TABLE 4.—*Mortality of Pneumococcus Types for Digitalis Untreated and Treated Cases*

	No Digitalis			Digitalis			
Type	Number of Patients	Number Died	Mortality, per Cent	Number of Patients	Number Died	Mortality, per Cent	Difference in Mortality
I.....	98	22	22.4	66	23	34.8	12.2
II.....	130	62	47.7	108	49	45.4	—2.3
III.....	28	9	32.1	25	12	48.0	15.9
IV to XIII and unclassified..	135	33	24.4	128	50	39.1	14.7
Miscellaneous..	13	10	....	11	6	....	....
Total.....	404	136	33.7	338	140	41.4	7.7

We have been unable to explain this inconsistency in otherwise consistent results. Our type II patients had similar age distribution in the two groups and the group receiving digitalis received it in the same dosage as did the patients having other types of pneumonia.

Our cases were carefully watched and toxic symptoms, such as vomiting, second, third or fourth stage

11. Brooks, Harlow: The Treatment of the Patient with Lobar Pneumonia, Internat. Clin. **4**: 201-215 (Dec.) 1927.

heart block and coupled rhythm, occurred to some degree in 75 of the 338 cases. As might be expected, 65 of these were noted in the 142 patients receiving digitalis B (the improperly standardized preparation), and in only 5 patients of the 93 receiving digitalis A, and in 5 of the 109 patients receiving digitalis G. These facts will be discussed later.

It was pointed out by Cohn and Jamieson [1] that, in auricular fibrillation and flutter, greatest benefit could be expected from digitalis therapy in pneumonia. Table 5 shows that in 835 cases there were 33 cases of either auricular fibrillation or flutter. Seventeen patients received no digitalis and 16 received it. Of the patients who received no digitalis, 9 died, a mortality of 52.9 per cent. Of the 16 patients who received digitalis, 14 died, a mortality of 87.5 per cent. In this

TABLE 5.—*Mortality and Incidence of Auricular Fibrillation and Flutter* *

Auricular Fibrillation and Flutter	No Digitalis (429 Patients)	Digitalis (406 Patients)	Total All Patients (835 Patients)
Number of patients	17	16	33
Incidence in series	4.0%	3.9%	4.0%
Number died	9	14	23
Mortality	52.9%	87.5%	69.7%

* The average dose of digitalis per patient for the digitalis treated group was 1.17 Gm.

paper these facts are simply being presented. A more detailed analysis of these cases and those now being studied will be presented at a later time.

Stone, Phillips and Bliss [7] discuss the necessity of considering separately patients the course of whose disease is associated with pneumococcal complications such as empyema, endocarditis, pericarditis, arthritis and meningitis from those not so associated. In order that we might do this, table 6 was prepared. This table shows that 27 of the digitalis treated patients had such complications; 19 died, a mortality of 70.4 per cent. There were 24 patients not receiving digitalis;

TABLE 6.—*Mortality of the General Series Except Patients with Pneumococcal Complications for Digitalis and No Digitalis Groups*

	No Digitalis			Digitalis			
Group	Number of Patients	Number Died	Mortality, per Cent	Number of Patients	Number Died	Mortality, per Cent	Difference in Mortality
General series	404	136	33.7	338	140	41.4	7.7
Pneumococcal complications	24	14	58.3	27	19	70.4	12.1
Series excluding patients with pneumococcal complications	380	122	32.1	311	121	38.9	6.8

14 died, a mortality of 58.3 per cent, a difference in mortality of 12.1 per cent in favor of patients not receiving digitalis.

A further study along this line is shown in table 7, which compares the mortality of patients with negative and with positive blood cultures. Of 53 patients with positive blood cultures who received digitalis, 42 died, a mortality of 79.2 per cent. Of 54 patients with positive blood culture who did not receive digitalis, 43 died, a mortality of 79.6 per cent, a difference of only 0.4 per cent in patients having positive blood cultures. On the other hand, of 116 patients having negative blood cultures and receiving digitalis, 40 died, a mortality of 34.5 per cent, while of 124 patients with negative blood cultures who did not receive digitalis, 25 died, a mortality of 20.2 per cent. This shows a 14.3 per cent lower mortality for those who did not receive digitalis.

TABLE 7.—*Comparative Mortality of Patients with Negative and Positive Blood Cultures for Digitalis and No Digitalis Groups* *

	No Digitalis			Digitalis			
Blood Culture	Number of Patients	Number Died	Mortality, per Cent	Number of Patients	Number Died	Mortality, per Cent	Difference in Mortality
Positive	54	43	79.6	53	42	79.2	—0.4
Negative	124	25	20.2	116	40	34.5	14.3

* Patients discharged at their own risk, and patients in the C and D (digitalis treated) series who received no digitalis have been excluded.

Table 8 compares the mortality of patients receiving the three preparations of digitalis and of patients taking none. It will be seen that the average cat unit dose of preparations A and G was 18.4 and 10.4, respectively, while that for preparation B, the misbranded one, was 31.3. It shows that the mortality rate of groups A and G are almost identical, 36.7 and 37.7 per cent, respectively, and that the mortality rate for patients receiving digitalis B is approximately 10 per cent higher, 47.2 per cent.

TABLE 8.—*Comparative Mortality of Patients Receiving Digitalis A, B and G and of Patients Receiving No Digitalis*

Digitalis	Average Cat Unit Dose	Number of Patients	Number Died	Mortality, per Cent
Specimen B	31.3	142	67	47.2
Specimen A	18.4	90	33	36.7
Specimen G	10.4	106	40	37.7
No digitalis	....	404	136	33.7

We expected an analysis of the latter group to show that the high mortality was due to the toxic effect of digitalis as shown by other evidences of digitalis toxicity, in which case, as is obvious, all patients receiving the drug in toxic dosage should not be considered in the investigation. Much to our surprise, however, we found that the highest mortality came in the group of cases that did not show any of the known toxic symptoms of digitalis but who had received large dosage of the drug. In fact, the analysis of table 9 shows that

TABLE 9.—*Mortality of Toxic and Nontoxic Cases*

Toxic	Number of Patients	Number Died	Mortality, per Cent	Average Cat Unit Dose
Specimen B	61	15	24.6	32.2 C. U.
Specimen A	5	2	40.0*	17.4
Specimen G	4	2	50.0*	8.0
All preparations	70	19	27.1	
Nontoxic				
Specimen B	81	52	64.2	30.6 C. U.
Specimen A	85	31	36.5	18.5
Specimen G	102	38	37.3	10.5
All preparations	268	121	45.1	

* Numbers too small to be of any significance.

patients developing signs of digitalis toxicity had not only a lower mortality (27.1 per cent) than patients receiving digitalis and developing no toxic signs (45.1 per cent), but even a lower mortality than patients receiving no digitalis whatever (33.7 per cent).

The possibility was considered of having included in the group receiving a large dosage of digitalis a number of patients who had actually received insufficient dosage of digitalis; in table 10 the nontoxic cases are further divided into those which showed positive digitalis effects on the T wave or the P-R interval in the electrocardiogram and those which showed no such effects. This table shows definitely that the higher mortality in the nontoxic digitalis group cannot be attributed to insufficient digitalis, because in the twenty-two patients who did not receive enough digitalis to produce an effect in the electrocardiogram, the mortality is low.

TABLE 10.—*Mortality According to Digitalis Effect All Preparations—Nontoxic Cases*

	Number of Patients	Died	Mortality
Digitalis effect	246	115	46.7%
No digitalis effect	22	6	27.3%

Because different preparations were given at various periods of the year and in different wards we have in table 11 compared the mortality rates of patients treated with each preparation of digitalis with those of the untreated patients for the same periods and on the same divisions. Thus the digitalis A cases are compared with the nondigitalis cases in the Third Medical Division up to Jan. 31, 1929, the digitalis B cases with nondigitalis cases of the First and Second Medical Divisions up to Jan. 31, 1929, and cases treated with digitalis G with the nondigitalis cases in all medical divisions after Jan. 31, 1929.

In this table an arbitrary grouping of the nondigitalis groups shows a range in the mortalities of these samples of from 30.8 to 36.4 per cent, a range of 5.6 per cent. The patients in the group receiving digitalis specimen A have a 0.3 per cent higher mortality, those receiving digitalis specimen G 6.9 per cent higher mortality and those receiving digitalis specimen B a 13.3 per cent higher mortality than a group treated under identical conditions and time, but receiving no digitalis.

TABLE 11.—*Comparative Mortality of Digitalis Untreated and Treated Patients According to Preparation Used*

	No Digitalis			Digitalis			
Period	Total	Died	Mortality	Preparation	Total	Died	Mortality
Divisions I and II; until Jan. 31, 1929	177	60	33.9%	Specimen B	142	67	47.2%
Division III; until Jan. 31, 1929	110	40	36.4%	Specimen A	90	33	36.7%
Divisions I, II and III; after Jan. 31, 1929	117	36	30.8%	Specimen G	106	40	37.7%
Entire period	404	136	33.7%	All preparations	338	140	41.4%

COMMENT

In the tables presented, in all categories except patients with type II pneumonia there was an increase in the mortality among patients receiving digitalis as contrasted with those who did not receive the drug. When these tables are reanalyzed, the patients receiving digitalis being grouped into those who received toxic dosage of the drug, those who received a digitalis effect but no toxic dosage, and those who showed no evidence of digitalis effect, it would appear that patients receiving enough digitalis to produce an effect on the electrocardiogram but not enough to produce toxic signs had an increased mortality, but on still further analysis it was shown that the increased mortality occurred in that group which received the largest amount of digitalis, irrespective of whether or not they showed toxic digitalis signs. Furthermore there is no evidence, even among the group who received what might be termed optimum dosage, that routine digitalis therapy could reduce mortality. This was true even among a small group of patients with auricular fibrillation who were studied.

In the giving of digitalis to patients with congestive heart failure in organic heart disease there are three guides useful in controlling medication: first, certain actions on cardiac mechanism, as shown clinically by ventricular slowing, or graphically by an increased P-R interval or changes in the T wave; second, the clearing up of signs of heart failure, and, third, the appearance of certain mild toxic phenomena. In pneumonia, on the other hand, except for the lowering of rate in patients who have developed auricular fibrillation there are practically no signs of digitalis effects other than those described in the electrocardiogram by Cohn and Jamieson [1] and toxic effects. The clearing up of signs of heart failure can never be used as a guide.

Since in the congestive heart failure of heart disease untoward effects are rarely if ever seen in patients who have not first developed mild symptoms of toxicity, it had previously been our belief that in patients with pneumonia receiving digitalis careful observation would give evidence of mild toxic digitalis effect before any damage could be done by the drug. This does not seem to be true in the light of our experience. In our cases there is a definite increase in the mortality of patients who received large doses of digitalis but who had none of the clinical symptoms of either early or late digitalis toxemia. May it not be that because of the effects of pneumonia toxin digitalis may produce death not infrequently without any warning signs of the usual clinical manifestations of mild or profound toxicity? If this is true, extraordinary care should be used in the giving of digitalis in pneumonia, for the dose cannot be guided except by an arbitrary limitation of the total dosage.

SUMMARY

There is no evidence that routine digitalis therapy in lobar pneumonia results in a lowered mortality.

In pneumonia patients with sinus rhythm the only consistent evidences of digitalis effect are electrocardiographic changes and mild toxic effects.

About 95 per cent of patients have sinus rhythm throughout the course of lobar pneumonia.

Clinical symptoms of digitalis toxicity are not a sufficient guide in digitalis therapy in lobar pneumonia to prevent increase in mortality when the drug is used. The amount of the drug given is a better guide.

When given in dosage too small to show any effect, it causes no changes in mortality. When given in dosage comparable with the amount usually needed in the treatment of heart failure, it produces effect on the P-R interval and T wave of the electrocardiogram but causes little change in mortality.

Digitalis may perhaps be life saving in an occasional patient in whom there is auricular fibrillation or auricular flutter.

Auricular fibrillation and auricular flutter occur rarely, in less than 5 per cent of all cases. Patients developing this condition frequently recover without digitalis.

It is believed by us that the routine giving of digitalis to patients with lobar pneumonia is dangerous.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. GOLD AND DEGRAFF AND DRS. WYCKOFF, DU BOIS AND WOODRUFF

DR. FRANK N. WILSON, Ann Arbor, Mich.: There has been a considerable difference of opinion among cardiologists regarding the advisability of giving digitalis in a routine manner to patients with pneumonia. Those who favored its administration advanced the following arguments: Digitalis has the same effect on the T-wave and the P-R interval of the electrocardiogram in pneumonia that it has in heart disease and in health (Cohn); consequently, pneumonia does not prevent it from producing its characteristic effects on the heart muscle. Auricular fibrillation is not uncommon in pneumonia. The response to digitalis is the same as in fibrillation due to other causes (Cohn). This disturbance constitutes an extra hazard which may be greatly diminished or eliminated by the routine administration of the drug. Roentgen studies have shown that the heart dilates in pneumonia. The dilatation is prevented or diminished by giving digitalis (Levy). The dilatation suggests that the heart muscle is weak; digitalis apparently improves its condition. Those who opposed the routine administration of digitalis in pneumonia did so on the ground that it had not been clearly shown that cardiac weakness played an important rôle in the mortality rate and that, as a general principle, drugs should not be given as a routine but only when the need for them became apparent. Those who favored giving the drug had, perhaps, a little the best of the argument; there was, however, something to be said on the other side. In view of the work which Drs. Wyckoff, Du Bois and Woodruff have reported, it is difficult, so it seems to me, to escape the conclusion that the routine administration of digitalis in pneumonia is dangerous. I should like to ask the authors their opinion regarding patients who have some measure of cardiac failure before they develop pneumonia; whether or not they advocate the giving of digitalis to these. If I understood Drs. Gold and DeGraff correctly, they dealt exclusively with patients who had auricular fibrillation. In such patients digitalis has a profound effect on the heart rate. This effect, which is a very important one in these patients, is due chiefly, not entirely, to the effect of the drug on vagal tone. In patients with normal rhythm, this effect is negligible. It is not known that the vagal and muscular effects of the drug are always parallel. Consequently, conclusions based on the effect of digitalis in one group of patients cannot, so it seems to me, be applied to the other without reservations.

DR. A. A. HEROLD, Shreveport, La.: In 1909 I read a paper before our state society in which I advocated the use of digitalis in pneumonia based on the fact that in numerous autopsies we found dilatation of the heart the cause of death in pneumonia. My plea at that time was to give the digitalis and feel the way both by blood pressure readings and by pulse rate, and give it, as Dr. Wilson brought out in summarizing the arguments pro and con, before it is too late, because if one waits for the fibrillation or the dilatation to start or what not and then starts digitalis, there will not be time to get the digitalis effect. That is a point which I would like to ask the authors to bring out in closing. How can a quick digitalis effect be obtained in those cases in which it is indicated if it is not going to be given in a routine manner?

DR. HAROLD E. B. PARDEE, New York: Drs. Gold and DeGraff have added an important fact to the knowledge of digitalis: the dose to maintain an effect need not be as large as the dose which was necessary to produce that effect. However, in its application to the therapeutics of digitalis, I do not believe that this is so important as it is from the point of view of pharmacology. In treating patients one is usually concerned with maintaining effects against rather considerable odds, and I would feel that in treating a patient it would always be necessary to give the patient the dose which would be close to his therapeutic limit before I would be sure that I had produced the best results of which the drug was capable. In the interpretation of the heart rate of patients with auricular fibrillation, certain sources of error arise, and these have a bearing on the conclusions of Drs. Gold and DeGraff. The chief source of error is that certain patients may have the same heart rate at rest and yet after exercise the heart rate will be increased differently, thereby indicating a different degree of digitalis effect. This may be in part due to an idiosyncrasy of the patient but it depends also on the degree of the digitalis effect. If a patient should be found with a heart rate when at rest of 75, which went up to 110 after a certain amount of effort, that patient given more digitalis might still have a heart rate when at rest of approximately 75, and yet after the same effort the rate would increase only to 90. Obviously the patient is in a much better physiologic condition when his heart rate goes only to 90 after exercise than he is when it goes to a higher rate, because exercise occurs constantly in his daily life. The heart rate cannot, of course, be taken as an indication of the degree of cardiac reserve. I believe that these two things also are so independent, in a considerable number of patients, that one must be wary how one draws conclusions from the heart rate as to the degree of cardiac reserve. Therefore, to maintain a constant heart rate when at rest does not necessarily men that cardiac efficiency is being maintained at a constant level or that the same therapeutic effect of digitalis is being obtained.

DR. OSCAR W. BETHEA, New Orleans: I was interested to note that the work on auricular fibrillation substantiated the work of the English physicians in which Lewis, following McKenzie, grouped the auricular fibrillation cases into four divisions: those that would remain normal when reduced to normal, without digitalis; those in which small doses of digitalis would maintain the effect; those in which large doses of digitalis were necessary to maintain the effect, and those in which no dose of digitalis would maintain the effect. I sometimes feel that we of this generation think that we discovered the large dose of this drug. I was interested recently to note that the elder Wood thirty odd years ago, in the United States Dispensatory, spoke of a patient that had received a teaspoonful of tincture of digitalis three times a day for a long period of years and had been maintained apparently in a state of perfect health. With regard to the treatment of pneumonia, I was highly delighted to note the trend of the statistics that were presented to us, particularly as in my paper tomorrow on the treatment of pneumonia, I protest most earnestly against the routine administration of digitalis.

DR. HARRY GOLD, New York: In reply to Dr. Wilson's remarks, I wish to say that we used only patients with auricular fibrillation in our study. Slowing of the heart rate in these patients is not due solely to stimulation of the vagus center. The evidence for that was presented many years ago by the results obtained after paralysis of the vagi by atropine in digitalized patients. Furthermore, slowing of the heart rate is only one element in the action of digitalis, and improvement that results in patients with auricular fibrillation is not due merely to slowing of the heart rate. The work of recent years has shown beyond a shadow of doubt that there is no fundamental difference between patients with a regular sinus rhythm and those with auricular fibrillation in the response of their congestive heart failure to digitalis. This suggests that the principles laid down in this study should apply to patients with a regular sinus rhythm. We were studying the response of heart failure to digitalis. Changes in the heart rate, however, yield the most striking graphic representation of the results and that is why we used the heart rate in our illustrations. We stated throughout that these patients improved as completely as possible and that when we gave them twice as much digitalis as they had at the beginning they did not show any greater improvement. I do not know what else one can do to ascertain that the full therapeutic effects of digitalis have been produced. Dr. Pardee's remarks on the relation between dosage and the response of the heart rate to effort are not supported by any evidence based on controlled studies. If a patient is given 3 grains (0.2 Gm.) of digitalis daily and marked improvement in the symptoms and signs of failure results, and if he is then given 6 grains (0.4 Gm.) daily with no signs of greater beneficial effects, it is probable that he does not need the 6 grains, but that 3 grains is sufficient. Dr. Pardee states that he prefers to give the larger doses. It is not justifiable to give patients twice as much digitalis as they need as a matter of personal preference, especially since we do not know what other actions, harmful or otherwise, the drug may exert in the body.

DR. JOHN HENRY WYCKOFF, JR., New York: In reply to Dr. Wilson's query about patients who have congestive heart failure or have heart failure before they develop pneumonia, I think that such patients should be treated as any other patients with congestive heart failure; they should be given digitalis. Dr. Herold asked how patients might be rapidly digitalized if such was necessary when routine digitalis therapy was not used. In cases of sudden death in pneumonia it seems to me that it is doubtful whether digitalis medication would ever be of value; for example, such a condition as ventricular fibrillation. But when heart failure does occur, as in the presence of auricular fibrillation, digitalis is probably indicated. Such an effect can be obtained by giving it by mouth in six to eight hours, or in one or two hours by the intravenous use of ouabaine. As to the value of digitalis in preventing cardiac dilatation, if digitalis does prevent such dilatation it should have had that effect in patients treated in this series as digitalis medication was begun as soon as possible after admission.

THE DRINKER RESPIRATOR

ANALYSIS OF CASE REPORTS OF PATIENTS WITH RESPIRATORY FAILURE TREATED FROM OCTOBER, 1928, TO JUNE, 1930 *

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In a series of papers published in THE JOURNAL [1] and elsewhere [2] we have given a description of the construction, operation and application of an electrically driven device for the prolonged administration of artificial respiration. As the result of considerable experience in the use of the apparatus in certain hospitals in Boston, New York and Philadelphia, various technical improvements have been made and a small respirator has been developed especially for the initiation of respiration of babies who breathe either with difficulty or not at all at birth. Both types of respirator, in their latest form, are shown in the accompanying illustrations.

Essentially, the respirator consists of a sheet metal tank equipped with a comfortable bed and mattress. The patient's head protrudes through a flat soft rubber diaphragm or collar attached to the body of the respirator, the rubber collar making an air-tight seal about the patient's neck. The diameter of the collar is adjustable, and thus excessive tension on the neck of the patient is avoided.

By means of electrically driven blowers and an appropriate valve arrangement, the air pressure within the tank is changed alternately from a few centimeters negative pressure to normal atmospheric pressure. The negative pressure induces inspiration—the chest and diaphragm of the patient expand and air is inhaled. The return to atmospheric pressure allows the normal tone of the respiratory muscles to cause expiration. Both the size and the rate of breaths taken are under control of the attendant and can be measured (or recorded) by means of a suitable U-tube manometer, filled with colored water and connected by rubber tubing to the body of the respirator.

In general, negative pressure of about 12 to 18 cm. of water suffices to maintain adequate ventilation in an adult or child with complete respiratory paralysis. In the case of new-born babies in which respiration does not begin within a few minutes after birth, lower negative pressures (from 8 to 10 cm.) have been found adequate.[3] Our experience indicates that the negative pressure used should be sufficient merely to prevent cyanosis or obvious respiratory distress—nothing is gained by using excessive negative pressures for long periods, while we have reason to believe that such pressures actually do harm to the lung tissue, particularly in the case of infants whose lungs may be atelectatic.[4]

Without having the pump stopped, the patients can eat, drink and sleep while in the respirator. A bed pan can be passed through one of the port-holes, enemas can be given, and rectal drips can be administered in deglutition cases. The noise of the machinery, although not excessive, is sufficient to prevent the use of a stethoscope in chest and heart examinations. We have taken roentgenograms of patients' chests both while the respirator was running and when the bed was pulled out and the pump stopped.

ANALYSIS OF CASE REPORTS

At this writing, June, 1930, twelve adult-sized respirators are in use in New York hospitals and two in Boston hospitals. One child's and three infant's respirators are in the Children's and Lying-In hospitals in Boston and two infant's respirators are in use in the University and Lying-In hospitals in Philadelphia. In all, approximately forty adult patients have been treated in New York; six adults, six children and about twenty-five infants (full-term and premature) in Boston, and three infants in Philadelphia. As the result of the simplification of the apparatus, treatment in the respirator has become more or less routine hospital procedure and does not require specialized attention on our part. It has therefore become increasingly difficult to obtain complete records of all cases treated. Our analysis consists of a brief summary of cases in which we have complete information and which we believe to be of interest to the medical profession.

Acute Anterior Poliomyelitis: Of seven desperate cases of respiratory failure treated, four have been described in THE JOURNAL.[1] Of the final recovery of one of these, B. H.,[1] Dr. Frank R. Ober, consulting orthopedic surgeon to the Peter Bent Brigham Hospital, Boston, May 24, 1930, writes:

It is impossible to say about B. H.'s ultimate recovery. When I first saw him on Sept. 26, 1929 [thirteen days after admission to the Peter Bent Brigham Hospital] he had a paralysis of practically every one of his skeletal muscles including the

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* Read before the Section on Preventive and Industrial Medical and Public Health at the Eighty-First Annual Session of the American Medical Association, Detroit, June 27, 1930.

1. Drinker, Philip; and McKhann, C. F.: The Use of a New Apparatus for the Prolonged Administration of Artificial Respiration, J. A. M. A. **92**: 1658-1660 (May 18) 1929. Wightman, H. B., and Shaughnessy, T. J.: A Case of Respiratory Failure Successfully Treated in the Drinker Respirator, ibid. **93**: 456-457 (Aug. 10) 1929. Shambaugh, G. E., Jr.; Harrison, W. G., Jr., and Farrell, J. I.: Treatment of the Respiratory Paralysis of Poliomyelitis in a Respiratory Chamber, ibid. **94**: 1371-1373 (May 3) 1930.

2. Drinker, Philip; and Shaw, L. A.: An Apparatus for the Prolonged Administration of Artificial Respiration: I. A Design for Adults and Children, J. Clin. Investigation **7**: 229-247 (June 20) 1929. Shaw, L. A., and Drinker, Philip: Ibid. **8**: 33-46 (Dec. 20) 1929.

3. Murphy, D. P., and Coyne, J. A.: The Use of a Modified Drinker Respirator in the Treatment of Asphyxia Neonatorum, J. A. M. A. **95**: 335 (Aug. 2) 1930.

4. Murphy, D. P.; Farber, Sidney; Drinker, C. K., and Drinker, Philip: Unpublished data.

muscles of his neck, back, thorax and abdomen, but not complete. His worst lesion was thoracic and abdominal. Associated with this paralysis he had marked tenderness of the lower extremities due to the peripheral neuritis which is so often associated with poliomyelitis. His chest expansion was less than one-half inch. October 3, his chest expansion was three-fourths inch and on October 10 it was 1⅛ inches. October 17, he was removed from the tank and his chest expansion dropped back to three-fourths inch. The tenderness in his leg muscles persisted until December 21, when physical therapy was started. He developed mild adduction contractures of both shoulders from exquisite tenderness and from the position in the tank. October 24, we put him back in the tank for short periods with the idea that the tank would relieve the fatigue of the chest muscles.

Today the contractures of his shoulders are about two-thirds eliminated and the power in the shoulder muscles is increasing. The power in his leg muscles has increased sufficiently so that he is able to walk about the house without any brace. His trunk muscles are still very poor, which interferes with his balance in walking. His chest expansion is now 2 inches. Crutches were necessary for some time but he no longer needs them except that he uses one to go up and down stairs, and he ought to be able to discard that.

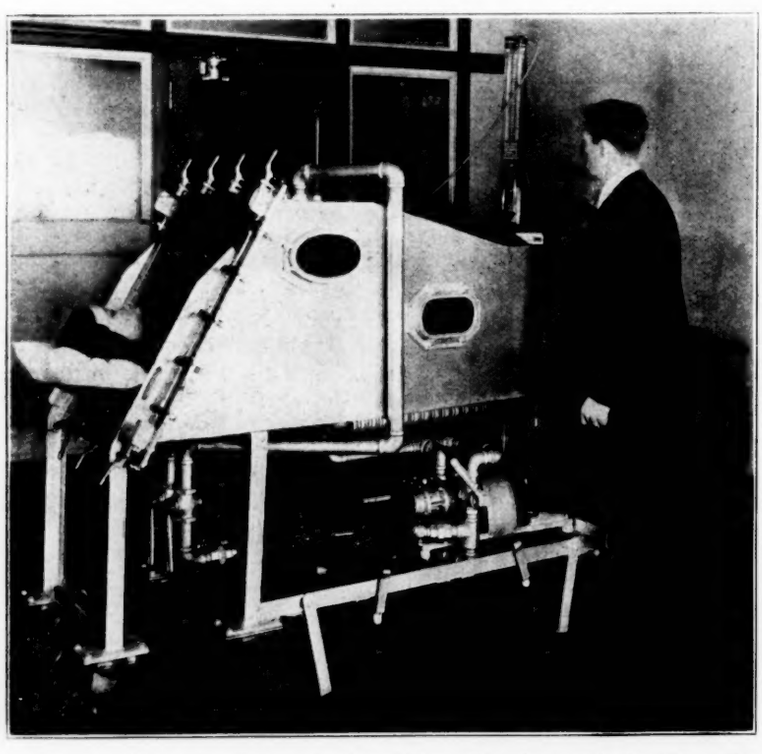

Fig. 1.—Adult-size respirator, showing rubber collar about patient's neck. The attendant is observing on the manometer the pressure within the respirator.

This boy has made a very marked and definite improvement since I first saw him in September. He has had daily physical therapy and only a slight amount of walking in the past few weeks and has had almost constant rest since he was first seen. He ought to gain constantly for an indefinite period. As to complete muscular recovery, I do not know, but functional recovery ought to be nearly normal.

A second case of poliomyelitis, in E. B., a boy, aged 10, has not yet been reported in the literature. Dr. Kenneth D. Blackfan of the Children's Hospital, Boston, and professor of pediatrics, Harvard University Medical School, under date of June 13, 1930, has written us about this child as follows:

I believe you should have the history of E. B., a boy of 9 years [on admission], who was treated in your respiration machine during the acute stage of infantile paralysis.

This boy was in good health until Sept. 16, 1929, when he complained of headache and stiff neck. He went to school but came home almost immediately and went to bed. He was feverish, irritable and nervous. That night he complained of pain in his back and he slept poorly. His condition remained about the same the next day. The third day a physician was called to see him. The diagnosis made at that time was infantile paralysis, established by the history, and paralysis of the left arm. September 19, the paralysis had spread to involve both arms and the intercostal muscles.

The child was seen at 2:30 a. m. by Dr. Aycock of the Harvard Infantile Paralysis Commission, who reported that the patient was "prostrated; flushed; restless; tremor. Rigidity of neck and spine; neck retracted; marked paralysis of both arms, paralysis of intercostal muscles; temperature 99.6 F.; pulse 138. Lumbar puncture: Pressure 200 mm. 'ground glass' appearance; cell count 112." Dr. Aycock obtained an ambulance and took the child and his father to the Children's Hospital (about seven hours' drive).

On admission, the boy's respirations were rapid and diaphragmatic in character. The chest did not move at all with inspiration. By this time the extremities had also become involved. He was removed to the respiration room, where he stayed for sixteen days. Throughout this time he was placed periodically in the respiration machine, spending about half the time in the machine during the first week and about one third of the time in it the second week.

While this boy at the time of admission was not in urgent need of artificial respiration, the effect of the assistance rendered by the machine was considered most beneficial as indicated (1) by the fact that the boy slept hardly at all outside the machine but would fall into a deep sleep as if exhausted when the assistance of the machine was given him; (2) the anxious attitude which he manifested when outside the machine was replaced by a sense of security; (3) the respirations were rapid, from 40 to 50, outside the machine, but were very much slower inside; lastly, and most important, after the first experience in the machine the boy periodically asked to be put in.

In the treatment of this child, negative pressure only was used, most of the time at —14 centimeters. The pressure was run to —30 occasionally, which disturbed the boy the first time it was done, but later he desired it this way when first put in the machine. The rate of artificial respiration was 35 the first day and from 25 to 30 thereafter.

Gradually his muscles returned so that it was no longer necessary for him to be kept in the tank and after the sixteenth day he was removed to the ward. Subsequently he was transferred to the orthopedic service, where treatment in the respiratory tank was continued in order to increase the chest expansion, and thus, if possible, to protect him somewhat against congestive, respiratory infections.

The subsequent course of the child has been given us by Dr. Arthur T. Legg, of the Children's Hospital, Boston, and Harvard Infantile Paralysis Commission, June 11, as follows:

When he was transferred to the orthopedic service E. B. had but one-half inch chest expansion. He was placed in the respirator periodically to rest the involved muscles and in the hopes that the action of the machine would develop chest expansion. At present he is able voluntarily to expand his chest 2¾ inches. He has not had any sign of a cold.

Four weeks ago I started another patient in the respirator. His paralysis began in 1927 and he had marked intercostal involvement. He has had many colds since that time and pneumonia on two occasions. He had an expansion of half an inch a month ago, since which time we have had him in the respirator twice a day (for a month). He now has a voluntary expansion of 1½ inches.

I believe the machine is going to be a wonderful asset in the after-treatment of intercostal muscles following infantile paralysis.

Our failures so far indicate that in bulbar involvement the respirator is apt to be ineffective. Also we have found that it is of the utmost importance occasionally but regularly to change the patient's position in order to prevent pulmonary congestion. For adults this means the development of a team, preferably of men, who call at scheduled times and do the necessary lifting and moving of the patient. At other times, a nurse in constant attendance has been found to be essential.

In general, it appears that respiratory failure in acute poliomyelitis is relieved and cyanosis is prevented. Whether or not a patient acutely ill will recover as the result of the respirator's having tided him over the most critical part of the illness is unpredictable.

Gas Poisoning (carbon monoxide).—In the emergency ward of the Bellevue Hospital, New York, the respirator is used two to three times each month (thirty-one cases since May, 1929). Of the forty cases in New York, seventeen have been gas poisoning (carbon monoxide). Nine of the patients recovered and were discharged from the hospital. In every instance inhalations of 95 per cent oxygen and 5 per cent carbon dioxide or 93 per cent oxygen and 7 per cent carbon dioxide were used before placing the patients in the respirator. Generally (and always in the emergency ward of the Bellevue Hospital), the oxygen and carbon dioxide mixture is used with the respirator when the patient is unconscious or when there is any evidence that the gas mixture is beneficial.

Most of the carbon monoxide cases are the result of attempted suicide, generally complicated by serious ill health. They are not typical "gas poisoning" cases. The usual type of accidental carbon monoxide poisoning can be treated fully as well by the oxygen and carbon dioxide inhalation method alone as by the respirator.

Alcoholic Coma.—Eight patients, seven in New York and one in Boston, were diagnosed as suffering from alcoholic coma and placed in the respirator when other resuscitative measures had proved inadequate. In two cases this diagnosis was complicated by the presence of drugs, and in one by carbon monoxide as well, and in another by a fractured skull. Of the eight patients treated, three recovered.

Drug Poisoning (morphine, heroin, barbital).—In New York, five patients with drug poisoning were treated in the respirator in the Bellevue Hospital. Of these, three recovered and one regained consciousness but died two days later. Of the three who recovered, the first had been reported in THE JOURNAL.[5]

Drowning.—One patient, a man, aged 45, was treated in the Bellevue Hospital. He recovered and was discharged.

Postoperative Respiratory Failure.—A woman, aged 22, was operated on for scoliosis. She had had poliomyelitis when a child, recovered, but grew up markedly deformed and with inadequate upper respiratory muscular control. At the time of her operation her normal respiratory rate was about 30; she was examined carefully and thought to be a good surgical risk. The operation (Hibbs') lasted approximately one and one-half hours. For the next two or three days she was anxious and apprehensive, with some cyanosis. On the eleventh day she became badly cyanosed and was unconscious when placed in the respirator. She regained consciousness quickly and then fell into a deep sleep. Because her heart was weak, pulse rapid and breathing dyspneic she was treated in the respirator constantly for ten days and at night for about one month; then she took naps in it twice daily for several weeks more. After two months she was taken home, although the condition of her heart was unsatisfactory. She died suddenly about three months after her operation. In this particular case it was apparent that the respirator always relieved cyanosis and caused a fall in pulse rate. When she was placed in the machine, her pulse rate would be about 140 and would gradually drop to about 120. So far this is the only case we have had in which the respirator apparently had a direct effect on the heart action.

Asphyxiation of the New-Born.—We are in entire agreement with the conclusions reached by Wachenfeldt[6] in the treatment of the axphyxiated new-born and particularly of premature infants, as shown in his recent discussion of the use of Thunberg's modified baby barospirator; namely, that there is a field for the device in the treatment of new-born babies in whom respiration is not initiated by the usual means.

Murphy and Coyne[3] have shown that natural respiration may be entirely absent for as long as one hour and eight minutes and only partially restored at the end of two hours and seventeen minutes, during all of which time the baby was kept alive in

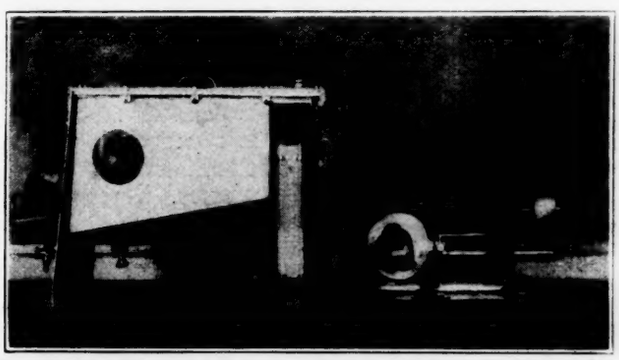

Fig. 2.—Baby-size respirator containing doll. The head end is hinged so that the angle of inclination of the baby may be adjusted; two 40-watt lamps are attached inside to furnish light and heat. Pump and valve are shown on the right.

the respirator. At the end of the two hour treatment the baby gradually resumed normal breathing and the respirator was stopped. The same investigators have shown also, and with this Wachenfeldt seems in agreement, that artificial respiration in atelectatic premature infants is extremely difficult. Whether the respirator has application in this problem we are in doubt, but it is hoped that cases of premature infants that have been treated will be reported later. Of such cases there are now a considerable number, but we cannot, at present, give the details.

We are indebted to Dr. Stewart H. Clifford, assistant visiting pediatrician to the Boston Lying-In Hospital, for the following account of the action of the respirator on a new-born baby:

A baby was born, severely asphyxiated, at the Boston Lying-In Hospital, May 26, 1930. The family history was unimportant. The mother was at full term and delivery had progressed in a normal fashion until the fetal pulse fell from 120 to 40 beats per minute. In order to save the baby the membranes were ruptured, an episiotomy was performed, and the baby was delivered without difficulty by pressure on the fundus.

5. Wightman and Shaughnessy (footnote 1).

6. Von Wachenfeldt, S.: Von der Wiederbelebung neugeborener, scheintoter Kinder-Versuche mit Thunberg's Barospirator (On the Resuscitation of New-Born, Apparently Dead, Children: Experiments with Thunberg's Barospirator), Acta obst. et gynec. Scandinav. **9**: 600-622, 1930.

At birth the baby was intensely cyanotic and the usual methods of resuscitation failed to stimulate respiration. After three or four minutes the baby was thought to be beyond hope but was placed in the respirator. The baby had not so much as gasped but as soon as the respirator was started the cyanotic color disappeared, and after three minutes the baby gave one gasp. The respirator was kept in operation for one and a half hours with the baby gasping every one to three minutes before he was able to maintain his own respiration. When the machine was stopped the respirations continued to be shallow and rapid. During the next eight hours the respirations ceased twice and the baby became intensely cyanotic, necessitating the use of the respirator.

Twelve hours after birth the baby was transferred from the respirator and lived for four days. During this time there were frequent cyanotic attacks and convulsions with breathing of the Cheyne-Stokes type. Lumbar, subdural and ventricle punctures showed normal fluid. Over the skin there were numerous petechiae but the rest of the physical examination was negative.

On the fourth day pneumonia developed, and the next day the baby died.

There was a postmortem which confirmed the clinical diagnosis of intra-uterine asphyxia with petechial hemorrhage into the various organs including the respiratory center.

Obviously this particular infant had no chance to live and I send you this note merely to show the action of the respirator on an asphyxiated infant.

COMMENT

We have often been asked: "What are the contraindications for the use of the respirator?" or, again, "Can it do harm?" We believe that contraindications are simply those of observing the patient's reaction to the respirator. If the patient is not suffering from respiratory difficulty or is not cyanosed, there is generally no point in using the respirator. If the patient does not respond to the treatment and does not spontaneously breathe in synchronism with the machine, the artificial respiration may actually interfere with his voluntary breathing and certainly does no good. Even in the case of conscious patients who are frightened and apprehensive but badly cyanosed, we have experienced no great difficulty in putting them into the respirator. A patient can be transferred from a bed or stretcher to the respirator very easily in less than one minute by inexperienced persons.

In many instances morphine has been given to patients who are already in respiratory difficulty but are apprehensive of the machine and are restless. This treatment has proved effective, especially in poliomyelitis, but obviously it is to be used only when the respirator is immediately available or when the patient has already been placed in it.

In the treatment of infants who do not respond to the customary respiratory stimuli at birth, the respirator seems particularly applicable. In such instances the machine must be near at hand, preferably in the delivery room or a room adjoining. A sufficient number of patients have been treated to indicate that, for the newborn, the respirator has a very useful field.

ABSTRACT OF DISCUSSION

DR. REGINALD FITZ, Boston: One of the most dreaded complications of acute poliomyelitis has been respiratory paralysis. One patient whom I saw would certainly have died had it not been for Dr. Drinker's machine. A young man with respiratory failure from infantile paralysis entered the hospital. He was at once put in the respirator. He soon was able to describe the benefit he received by it. When he was first taken out of it, he became apneic. Gradually he grew better and after living in the machine for a few weeks was able to be out of it for a few minutes at a time without discomfort. Now he is perfectly all right as far as his respiration is concerned. I believe that this machine is going to have considerable clinical importance in the future, especially in any general hospital that is likely to have an accident room service, for it is in the accident room that emergency cases will enter with various types of inability to breathe. Certainly, in acute poisoning cases in which there is respiratory failure the machine ought to be of distinct practical value, for in these it is largely a question of tiding the patients over a comparatively short time before recovery occurs. If there are to be epidemics of infantile paralysis in the future, hospitals treating such cases should be equipped with the respirator. One life saved is worth a lot, and it is comforting, at least, to have something in the line of rational therapy to offer those cases of respiratory failure which heretofore were doomed. I was rather doubtful about the machine at first. It looked cumbersome, it was noisy, and it seemed more like a torture chamber than anything else, but certainly the one boy that I saw get well in it entirely convinced me as to the practical value of this method of giving artificial respiration.

DR. W. LLOYD AYCOCK, Boston: From the point of view of the ultimate outcome of the disease, paralysis may be divided into two kinds: Permanent paralysis, certainly due to the destruction of the motor cells in the spinal cord, and temporary paralysis, undoubtedly due to a temporary interference with nerve cells which are not actually destroyed. Temporary paralysis is seen in all parts of the body. Every patient with infantile paralysis who survives undergoes improvement to a greater or less extent in the actual amount of paralysis. One of the most striking examples of temporary paralysis is seen in a type of case which is becoming more frequent; namely, paralysis of the swallowing mechanism. Many of these patients are completely unable to swallow for four or five days, after which they recover entirely. When temporary paralysis involves a group of muscles that are not absolutely essential to life, there is no danger to the patient. A patient can live five days without swallowing. But when the paralysis involves a vital group of muscles, such as the muscles of respiration, the patient cannot survive cessation of the use of these muscles for any length of time. As a matter of fact, when the intercosal muscles and the diaphragm become paralyzed, these patients undertake to give themselves artificial respiration by means, first, of their neck and shoulder muscles, and then the muscles of the mouth. Of course, they cannot keep this up for any length of time. Many devices have been tried for aiding the patient with this artificial respiration. None have ever been successful, owing, primarily, to the violation of the principles of respiration, and, secondly, to the fact that one is dealing with a perfectly conscious patient who realizes his breathing difficulty and who will not permit any muzzling of his face when he is in this condition. Early in Dr. Drinker's work on this machine, we were fully convinced that it might serve the desired purpose in infantile paralysis, and we have used it in several cases. We can't predict in any case whether there will be a return of function. None of the signs or symptoms give any indication of the ultimate extent or outcome of paralysis, so the best we can do is to give all these patients the benefit of the doubt. Some of them undoubtedly will resume their muscle power while others may not. It may seem like an emergency measure that cannot be made available to any extent, but with a few of these machines stationed at central points, it is not difficult to get a patient to the machine. I was called to Vermont last fall to see a suspected case back in the hills. I found this boy with a beginning intercostal paralysis. We got him to Boston, a matter of a seven hours' ride, and into this machine. He had been lying awake for many hours; as soon as the machine started he fell sound asleep. We stopped the machine and immediately he woke up. We started it again and he went back to sleep. We tried this several times. This boy has now made quite a remarkable recovery. The point is that in respiratory paralysis the patient has to use voluntary effort to keep up breathing. To one whose job it has been to sit by these gasping, moribund patients, to see them immediately take on

the aspects of a perfectly well person when placed in the respirator is gratifying.

DR. MILLARD KNOWLTON, Hartford, Conn.: I should like to ask Dr. Drinker the cost of the apparatus.

DR. WILLIAM R. REDDEN, New York: In 1927, a rescue squad which I had trained in Youngstown, Ohio, was called on to give artificial respiration to a victim of Landry's paralysis which had gradually involved the diaphragm. The men continued artificial respiration for about twenty-eight hours during which time the victim remained conscious. Eventually, as was to be expected, he died. The description members of the rescue squad gave me of the discomfort and even agony that this victim suffered from the application of artificial respiration by manual pressure made me realize that any type of apparatus such as Dr. Drinker has developed has marked value. In the case mentioned, and in similar cases, the Schaefer method of artificial respiration is out of the question because no conscious person can tolerate the amount of pressure used in this method for more than an hour, at least not without great shock. For this reason, none of the usual forms of artificial respiration are used, but the victim is placed on his back in a comfortable position on a table or bed, and then manual pressure is applied simultaneously at the anterior costal margin by two operators, one standing on each side. Even this greatly modified manual pressure method soon becomes almost unbearable for the conscious victim. Therefore, any type of respiratory failure which may require prolonged artificial respiration, but especially those in which the victim remains conscious, should be treated as soon as possible in a machine like Dr. Drinker's, which does no damage to the victim, which causes no pain or distress, and which even allows the victim to sleep. Aside from its use in respiratory failure, let me suggest that sleepless patients, instead of being given drugs, be put in this machine and the blood oxygenated, and I am sure they will drop off to sleep without trouble.

PHILIP DRINKER, PH.D., Boston: Answering Dr. Knowlton's question about cost, the adult size machines are sold for $2,000. Dr. Redden mentioned Landry's paralysis. Recently I was called in an emergency to the Boston City Hospital and used the respirator in a case of Landry's disease. All we accomplished was to make the woman comfortable; she died gradually. I understand that in Landry's paralysis recovery is unknown. I did not mention that we know the apparatus can do harm under certain conditions. This we found through animal experimentation and not on patients. We curarized animals and then subjected them to more pressure than was necessary merely to sustain life. If the animal lay tilted head downward we found we could use higher negative pressures than if the animal lay horizontally. As a result, we have arranged the baby respirator so that excessive pressures cannot be obtained and do not let the baby machines go to hospitals until the danger from using excessive pressures is understood. In animals examined post mortem the damage, if any, is grossly apparent in the dependent portions of the lungs. Patients remaining in the respirator for twelve hours or longer require a trained crew who can either take them out, turn them over and put them back in the machine again, or else, if the space within the machine permits, put in side boards by the patient's side and tilt him first to one side and then to the other, just as one would in postoperative recoveries.

Medicine and Science.—The practice of medicine in its broadest sense includes the whole relationship of the physician with his patient. It is an art, based to an increasing extent on the medical sciences, but comprising much that still remains outside the realm of any science. The art of medicine and the science of medicine are not antagonistic but supplementary to each other. There is no more contradiction between the science of medicine and the art of medicine than between the science of aeronautics and the art of flying. Good practice presupposes an understanding of the sciences which contribute to the structure of modern medicine, but it is obvious that sound professional training should include a much broader equipment.—Peabody, F. W.: Doctor and Patient, New York, Macmillan Company, 1930.

LYMPHATIC LEUKEMIA

WITH GENERALIZED FOLLICULAR ERUPTION OF TUBERCULOMATOUS ARCHITECTURE *

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AND
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PITTSBURGH

An extensive literature has accumulated on the classification and interpretation of diseases of lymphatic origin. Cutaneous reactions occur in both general types of leukemia but are notably more common in the lymphatic variety.

Cutaneous and subcutaneous changes are occasionally noted at some time during the course of many diseases of the hematopoietic system. This is especially true

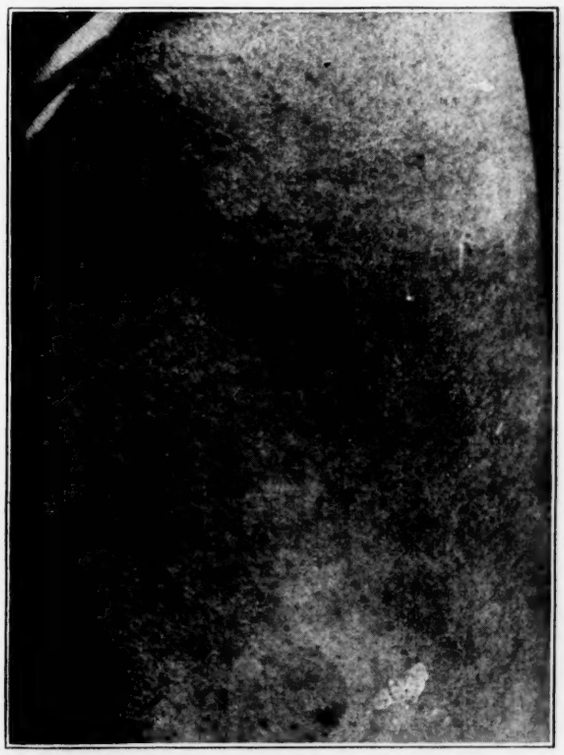

Fig. 1.—Follicular papular eruption on inner aspect of left thigh.

in that closely allied group of diseases designated by Keim [1] as the lymphoblastomas, including leukemia, mycosis fungoides, lymphosarcoma and Hodgkin's disease. Arndt,[2] in 1914, classified the visible expressions of the leukemias in two classes: first, the diffuse or circumscribed true lymphadenoses and, second, a multiform type of lesion which did not represent a true leukemic infiltration and which was indistinguishable from the toxic dermatoses of different origin. The latter were designated as the leukamids. It is concerning this class that much further elucidation is needed. The following case is reported for the reason that the unusual relationship of a blood picture of a

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* Read before the Section on Dermatology and Syphilology at the Eighty-First Annual Session of the American Medical Association, Detroit, June 26, 1930.

1. Keim, H. L.: Universal Leukemia Cutis, Arch. Dermat. & Syph. **10**: 579 (Nov.) 1924; The Lymphoblastomas, ibid. **19**: 533 (April) 1929.

2. Arndt, G.: Diseases and New Growths of Lymphatic Origin, J. A. M. A. **63**: 1268 (Oct. 10) 1914.

chronic low grade lymphatic leukemia and a papular eruption of tuberculomatous structure may add something to clarify this picture.

REPORT OF CASE

History.—J. M., a white woman, aged 53, American born, a housewife, had had the usual diseases of childhood and typhoid at 20; otherwise her personal history was unimportant. Her

Fig. 2.—Infiltrate about the sweat duct and vessels and early formation of epithelioid cells in the lower cutis; × 100.

mother and father had both died, but the cause was not elicited. Three brothers were living and well. She had no sisters. There was no history of tuberculosis, cancer, nephritis, syphilis or insanity.

Present Illness.—The present illness began in the spring of 1926. It began as a slight follicular papular eruption on the trunk. The patient did not consult her physician regarding it until June, 1928, at which time she also suffered with backache. Laboratory tests at that time revealed a negative blood Wassermann test and a negative urinalysis. Blood examination revealed hemoglobin, 98 per cent; red blood cells, 4,930,000 and white blood cells, 20,900 per cubic millimeter. The differential count showed; polymorphonuclear leukocytes, 22.5 per cent; lymphocytes, 77.25 per cent, and basophils, 0.25 per cent. Roentgenograms of the lumbar and sacro-iliac regions showed no evidence of abnormality in the bones of the lower dorsal or lumbar region. The joint margins of the sacro-iliac joints showed an increase in bone density suggestive of bone sclerosis, which might lead one to believe that there existed a chronic arthritis involving the sacro-iliac joints. Dental roentgenograms were made of all teeth, and three periapical abscesses were revealed. These teeth were promptly extracted and the abscesses removed by curettement, July 31, 1928, she was referred to us by David M. Bell, M.D., of Canonsburg, Pa.

Cutaneous Examination.—The entire skin surface of the trunk, arms and legs was covered with a fine follicular papular eruption (fig. 1). The individual lesion was a very small keratotic papule, capped with a small horny spine which could be removed only with considerable difficulty. Each papule was surrounded by a small margin of erythema. Over the arms, legs, upper back and neck, the lesions were all distinctly discrete. On these areas, the lesions resembled very much the characteristic papules of keratosis pilaris. The papules were more closely studded and more abundant on the flexor surface of the extremities rather than over the extensor (keratosis pilaris) surface. On the lower part of the trunk (around the back and abdomen) the spines appeared to have been rubbed off. The papules were larger and flatter, and there appeared more of a tendency to but no actual confluence of lesions. Also here they were yellower or more apple jelly-like in quality. The face, palms, soles and the dorsal surfaces of the fingers and toes were free from lesions. There was no caputal, pubic or axillary alopecia. The condition was only mildly pruritic and there was no thickening or excoriation or trauma due to excessive scratching.

Physical Examination.—The patient was of medium height, weighed 135 pounds (61.4 Kg.) and was well nourished. The eyes, ears, nose and mouth were normal. The thyroid gland was not enlarged. There was a single, discrete, palpably enlarged gland in the left anterior cervical chain. Other glands were not enlarged. Her heart and lungs were normal except for a mild atherosclerosis not unusual in patients of her age. Her liver was palpable at the costal margin. The spleen was enlarged to percussion only. Laboratory study showed a basal metabolic rate increased 9 per cent; urinalysis was normal; the phenolsulphonphthalein excretion was 39 per cent in two hours; the nonprotein nitrogen was 31.5 mg. per hundred cubic centimeters; urea nitrogen, 11.5 and blood sugar 97. Blood examination showed: hemoglobin, 80 per cent; erythrocytes, 5,650,000 per cubic millimeter; white blood cells, 2[illegible],400. The differential count was: polymorphonuclear neutrophils, 12 per cent; eosinophils, 1 per cent; small lymphocytes, 8[illegible] per cent; large lymphocytes, 3 per cent, and transitionals, 1 per cent. Many cells were embryonic in type.

The diagnosis of a consultant internist was that of "typical chronic low grade leukemia." The patient was presented before the Pittsburgh Dermatological Society, and Hollander[3] voiced the opinion of those present that it was a most unusual and interesting case. A section of skin containing many typical papules was removed for study.

Pathologic Examination.—The following report was submitted by Dr. H. H. Permar, pathologist of the Mercy Hospital:

Macroscopic History: The specimen was of a small elliptic piece of skin from the chest, measuring 1 by 0.5 cm. and having a thickness of 0.5 cm. The material was received after fixation, and in that state it failed to show the small superficial lesions noted in the clinical history.

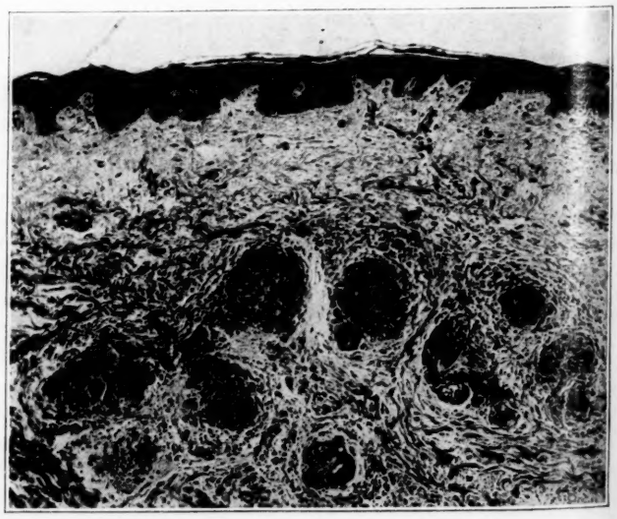


Fig. 3.—Typical tuberculoid structure. The tubercle at the left shows early central caseation. A hair follicle is shown in the lower center; × 100.

Microscopic History: Sections of the skin showed foci of chronic inflammation which were clearly granulomatous in type (fig. 2). They lay in the corium and tended to be fairly close to the epidermis. (In one place the papillae of the malpighian layer were distinctly flattened over the inflammatory area, and

3. Hollander, Lester: Transactions of the Pittsburgh Dermatological Society, Arch. Dermat. & Syph. **19**: 326 (Feb.) 1929.

the epidermis was thin with some increase in the amount of keratin [figs. 3, 4 and 5].) This probably represented one of the small keratotic papular lesions.

The granuloma had the classic histologic picture of miliary, submiliary and early conglomerate tuberculosis. The inflammatory nodules were made up of flattened or ovoid epithelioid cells having an irregularly concentric arrangement about small centers of early caseation necrosis (fig. 6). Typical Langhans

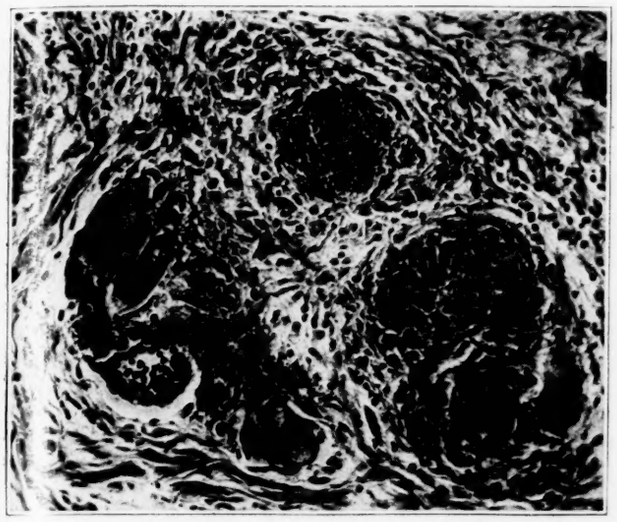


Fig. 4.—A portion of figure 3. Note lymphatic or blood vessel in lower left hand corner which is packed with immature white blood cells; × 2[illegible].

giant cells were located eccentrically in the nodular foci and were not seen in every one. The larger foci showed a few polymorphonuclear leukocytes lying in the areas of early caseation necrosis. Zones of lymphocytes encircled the rounded masses of epithelioid cells, and just beyond these the nodules were demarcated by a zone of fibrous tissue. The vessels of the corium showed collections of lymphocytes and plasma cells lying in the perivascular lymphatics and in the stroma about them; and the sweat glands were surrounded by similar cell collections, again evidently in lymphatics (figs. 7 and 8). An occasional small lesion, perfectly characteristic of a miliary tubercle, was found along the course of the lymphatics in the corium, often at some distance from the larger foci.

The diagnosis was tuberculosis of the skin of the chest.

Treatment, Clinical Notes and Progress.—Although we were unable to demonstrate whether the pathologic blood picture was the primary disease and the skin expression secondary or vice versa, we felt as the internist and hematologist did that we were dealing with a leukemic syndrome. From her first visit, July 31, to Aug. 27, 1928, only internal tonic medication and local soothing applications were administered.

She was then given four one-half skin unit roentgen-ray exposures, one half of the body surface being irradiated weekly such that the total consisted of one skin unit to the entire body surface. Following this treatment there was an initial rapid fall in the white blood count. The differential count also showed a rise in polymorphonuclear leukocytes and a fall in lymphocytes. At the time the smear also showed many degenerating white blood cells, largely of the lymphocytic type. There was likewise a corresponding resolution in skin lesions and less itching.

September 27, intramuscular injections of spleen extract were begun. These were continued for a total of twenty-four semiweekly, weekly or biweekly injections. During this period the patient's blood picture gradually became normal, as shown in the accompanying table.

COMMENT; DIFFERENTIAL DIAGNOSIS

Cutaneous and subcutaneous changes have been so frequently reported in connection with the lymphoblastomas that we consider it needless here to enter into a complete discussion of these various cutaneous expressions in the form of leukamids and true leukemic infiltrations so ably described by Arndt, Keim and others.

In no case that we have reviewed has there been described a skin lesion associated with a leukemic blood picture which showed the clinical or histopathologic architecture of our case. The blood picture is definitely that of a chronic lymphatic leukemia. This point of view was substantiated by Dr. George Kastlin, hematologist at the Mercy Hospital. The histologic picture is not that of a true leukemic infiltration of the skin. The pathologic changes in the circumscribed type consist of a dense infiltrate of small or large lymphocytes, located principally around the blood vessels, the follicles and glands. There is an edematous zone of noninfiltrated tissues between the reticular layer and the epidermis; a very little increase in connective tissue, and a loss of elastic tissue and pilosebaceous structures in the larger tumors. In the diffuse type of leukemia cutis, the pathologic changes are quite similar except that the infiltrative process is general. The leukamids are associated with but do not present a histologic picture of a true leukemia. They are supposedly the result of an intoxication from the underlying leukemia and show themselves as petechiae, papules, vesicles, wheals, nodules, pigmentation, exfoliation or a simple general pruritus. In no instance have we found a description of a leukamid as a spine capped papule with a histologic picture of tuberculosis.

Gans [4] describes the leukamids as nonspecific reactions in myelosis and lymphadenosis. He says, "The nonspecific variety bears but loose relationship to the underlying disease and needs further elucidation."

Fig. 5.—Taken where the epidermis was flattened and it showed several tubercles, one near the hair follicle; × 75.

It is of interest here to refer to the study of Michelson [5] on the occurrence of tuberculoid reactions

4. Gans, Oscar: The Skin Picture in Hematopoietic Diseases, Arch. Dermat. & Syph. **16**: 1 (July) 1927.

5. Michelson, H. E.: The Occurrence of Tuberculoid Reactions in the Inguinal Glands in Early Syphilis, Arch. Dermat. & Syph. **19**: 66 (Jan.) 1929.

in the inguinal glands in early syphilis. Of twenty-nine cases of early syphilis in which the inguinal glands were examined, tuberculoid reactions were observed in eight. Two types of tuberculoid reactions were noted, the so-called epithelioid or indurative tuberculoid structure involving almost the entire node, and a second type likened to that found in miliary tuberculosis.

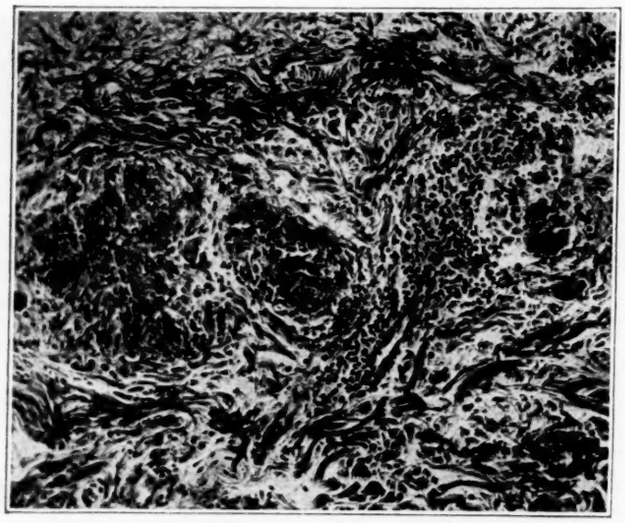


Fig. 6.—On the left, tubercle with early central caseation necrosis; epithelioid cells about the blood vessel in center, and a perivascular infiltrate of cells of the lymphocytic series, extending diagonally across the right side; × 150.

Professor Bloch [6] in discussing this report, stated that this structure was not specific for a tuberculous infection but that it could be found in many diseases, such as in leprosy, tertiary syphilis, sporotrichosis, trichophytosis and blastomycosis. He says, "The rule that tuberculous structures are found not only in tuberculosis but in many other infections, when allergic conditions are present, is not sufficiently known and considered by pathologists."

Clinically the lesions are rather suggestive of a generalized lichen scrofulosorum. The papules were follicular and capped by a horny spine. Around the lower trunk there was some tendency to flattening. The lesions were yellowish and waxy in color and covered by minute scales. On the other hand, there was no tendency whatever to grouping. Also the eruption was almost uniformly distributed over the entire trunk and extremities. The age of the patient was somewhat over the usual age incidence of lichen scrofulosorum. Careful clinical and roentgen examination failed to reveal any evidence of active or healed tuberculosis.

Histologically, the sections showed numerous giant cells and caseation necrosis. Pusey [7] states that "most observers have demonstrated the presence of giant cells, but other elements of the typical tuberculous process, such as coagulation necrosis and caseation, have not been observed in lichen scrofulosorum." Wise [8] and Michelson [9] reported that small areas of caseation occurred in some cases but that ordinary inflammatory changes are found more frequently than the tuberculoid structure. Plasma cells are rare.

6. Bloch, in discussion on Michelson (footnote 5).
7. Pusey, W. A.: The Principles and Practice of Dermatology, ed. 4, New York, D. Appleton & Co., 1924.
8. Wise, Fred: Miliary Tuberculosis of the Skin, Lichen Scrofulosorum, and Papulotuberculosis, J. Cutan. Dis. **37**: 105 (Feb.) 1919.
9. Michelson, H. E.: Lichen Nitidus, Arch. Dermat. & Syph. **7**: 763 (June) 1923.

Towle and Swartz,[10] in studying the blood count in tuberculosis of the skin in twenty-five cases, report the total white count ranging from 7,000 to 15,000. The average normal was 10,360. The polymorphonuclears ran as low as 1,320 and as high as 10,530. The average was 6,392. The highest lymphocyte count was 8,760, the lowest 4,000, with an average of 3,299. Mononuclears were low, with a total average of less than 300. These figures seemed to agree with the figures in internal tuberculosis.

Pityriasis rubra pilaris must be considered in the differential diagnosis of a general follicular papular dermatosis of this type. In our case there were no lesions of the proximal phalanges, nor was there any alopecia. The lesions were discrete, with no tendency to coalescence at the end of two years' duration. The true tubercular histopathology and blood picture also do not fit in with this condition.

The blood picture of a chronic lymphatic leukemia and the tuberculomatous architecture of the skin lesions differentiate it from such conditions as lichen planus, lichen nitidus, lichen spinulosus, follicular syphilids, trichophytids and other follicular papular dermatoses.

The case is unique in that it showed the blood picture of a chronic lymphatic leukemia associated with a follicular papular cutaneous eruption with a true tuberculomatous structure. We are unable to demonstrate positively which one of the two pictures was primary. The case can be argued as one of a chronic lymphatic leukemia and the skin picture as a leukamid. Although the leukamids are supposedly toxic or allergic expressions of the underlying blood dystrophy, little is known of the actual histopathology of these lesions. In view of Michelson's observations in syphilis and Bloch's reference to tuberculoid reactions to allergy, it is logical to presume that the tuberculomatous structure of the

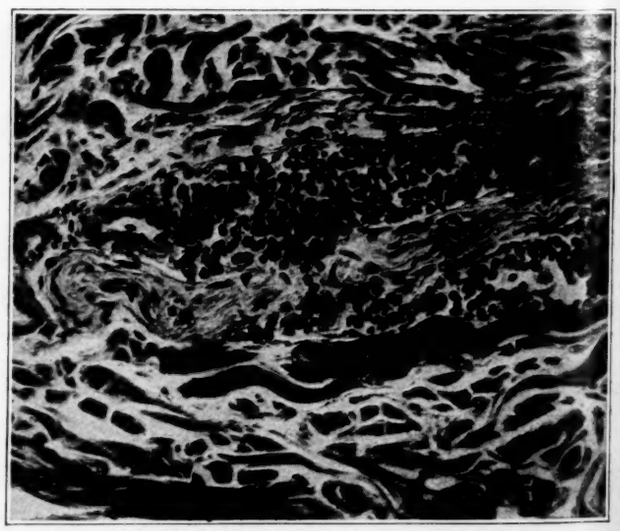


Fig. 7.—Character of the infiltrate about the arrectores pilorum muscle; × 300.

cutaneous lesions in our case is an expression of an allergic nature.

Considering the existence of a mild lymphocytic leukocytosis in cutaneous tubercular structures, one must analyze the condition as a tubercular skin eruption, possibly generalized lichen scrofulosorum. The histo-

10. Towle, H. P., and Swartz, J. H.: A Study of the Blood in Some Common Diseases of the Skin, Arch. Dermat. & Syph. **9**: 554 (May) 1924.

pathologic architecture in which there is tubercle formation with giant cells and coagulation and caseation necrosis, so dominant a feature, is not that of the usually accepted pathology of lichen scrofulosorum. The abnormally high leukocyte count is out of proportion to blood counts reported in association with cutaneous tuberculosis. Also, the age of the patient, the absence of grouping, and the lack of any collateral evidence of tuberculosis argues against the skin picture as being the primary feature in this case. The associated blood and clinical picture reasonably excludes the other follicular papular cutaneous possibilities.

Regarding the almost miraculous response to treatment we are unable to conclude whether the entire course of progress was the result of the roentgen treatments or of the subsequent injections of spleen extract. The use of spleen extract in allergic dermatoses was first reported by Leo von Zumbrusch[11] of Munich. Having observed that splenectomized animals and eczematous patients both have eosinophilia, and that roentgen stimulation of the spleen resulted in improvement of eczematous lesions, an albumin free extract of hog spleen was administered with astonishing results to patients with eczematous lesions. Paul[12] reported striking results from the use of spleen extract in a series of cases of eczema, urticaria, pruritus ani, asthma, lichen planus, miliaria and psoriasis.

Beinhauer[13] obtained a rapid relief of pruritus and a sharp decrease in eosinophilia in a series of cases in which spleen extract was used. Although our case did not show an appreciable eosinophilia, the possible allergic tuberculomatous type of skin lesion associated with the blood picture of a hematopoietic disease led us to use spleen extract as a therapeutic agent.

SUMMARY

We report an unusual case with a generalized follicular papular eruption. The individual lesion was a discrete keratotic papule capped by a small horny spine and surrounded by a narrow erythematous margin. The histopathologic structure was that of miliary, submiliary and early conglomerate tuberculosis.

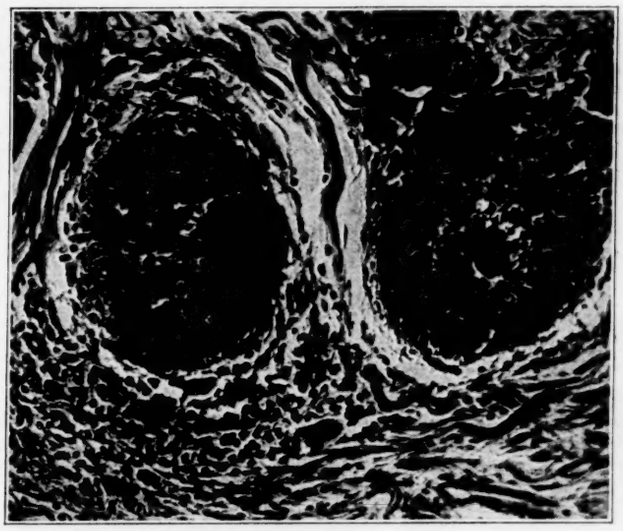


Fig. 8.—A poor photomicrograph which shows early central zone of caseation and peripheral zone of lymphocytes about one of the tubercles; × 250.

Treatment and Blood Picture Chart

Date	Treatment	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Polymorphonuclear Neutrophils, per Cent	Basophils, per Cent	Eosinophils, per Cent	Small Lymphocytes, per Cent	Large Lymphocytes, per Cent	Transitionals, per Cent
6/ 4/28	.....	98	4,930,000	20,900	22.5	0.25	..	77.25		
7/31/28	.....	80	5,650,000	24,400	12	..	1	83	3	1
8/20/28	.....	..	.....	19,900	19	..	1	52	23	5
8/30/28	X-ray.....	..	.....	20,300	23	..	..	67	15	5
9/ 4/28	X-ray.....	..	.....	13,700	38	..	..	46	11	5
9/10/28	X-ray									
9/13/28	X-ray.....	..	.....	12,300	40	..	2	50	3	5
9/27/28	Spleen extract 1 cc.	..	.....	12,300	43	..	2	46	7	2
10/ 1/28	Spleen extract 1 cc.									
10/ 4/28	Spleen extract 2 cc.	..	.....	12,200	49	0	0	42	7	2
10/ 8/28	Spleen extract 2 cc.									
10/11/28	Spleen extract 2 cc.	..	.....	9,250						
10/16/28	Spleen extract 2 cc.									
10/19/28	Spleen extract 2 cc.	..	.....	10,550	53	0	1	40	3	3
10/23/28	Spleen extract 2 cc.	..	.....	9,600						
10/26/28	Spleen extract 2 cc.	..	.....	7,500						
11/ 2/28	Spleen extract 2 cc.	..	.....	9,600						
11/ 9/28	Spleen extract 2 cc.	..	.....	8,500	45	..	3	40	8	4
11/14/28	Spleen extract 2 cc.									
11/21/28	Spleen extract 2 cc.	..	.....	8,800	53	..	..	40	5	2
11/28/28	Spleen extract 2 cc.									
12/ 5/28	Spleen extract 2 cc.	..	.....	8,600						
12/12/28	Spleen extract 2 cc.									
12/26/28	Spleen extract 2 cc.	..	.....	8,400	66	0	6	20	6	2
1/ 9/29	Spleen extract 2 cc.	..	.....	7,500						
1/23/29	Spleen extract 2 cc.									
2/ 6/29	Spleen extract 2 cc.	..	.....	7,400	58	1	2	31	7	1
2/22/29	Spleen extract 2 cc.									
3/ 8/29	Spleen extract 2 cc.	..	.....	7,000						
3/20/29	Spleen extract 2 cc.									
4/12/29	Spleen extract 2 cc.	..	.....	6,900						
6/ 4/29	Spleen extract 2 cc.	..	.....	8,500	60	0	4	30	12	4
7/22/29	Spleen extract 2 cc.	..	.....	7,000						
10/ 9/29	.....	90	.....	9,250	52	..	3	32	10	3
11/ 2/29	.....	..	.....	6,800						
12/ 6/29	.....	..	.....	7,000						
1/29/30	.....	100	4,580,000	7,900	55	0	0	22	14	9
4/ 9/30	.....	85	4,100,000	7,500	60	0	1	30	8	1

There was an associated blood picture of a typical chronic low grade leukemia. The blood showed: hemoglobin, 80 per cent; erythrocytes, 5,650,000; white blood cells, 24,400 per cubic millimeter. The differential count was: polymorphonuclear neutrophils, 12 per cent; eosinophils, 1 per cent; small lymphocytes, 83 per cent; large lymphocytes, 3 per cent, and transitionals, 1 per cent.

11. Von Zumbrusch, Leo: The Question of Eczema and the Exudative Diathesis, Urol. & Cutan. Rev. **31**: 750 (Dec.) 1927.
12. Paul, T. M.: The Instantaneous-Physiologic Cure of Eczema and Urticaria, Urol. & Cutan. Rev. **33**: 724 (Nov.) 1929.
13. Beinhauer, L. G.: Personal communication to the authors.

After roentgen-ray exposure of one skin unit in divided doses to the entire skin surface, there was a rapid decrease in leukocytosis and improvement in the relative percentages of white blood cells.

During and after a total of twenty-four semiweekly, weekly, or biweekly injections of spleen extract, the cutaneous and blood pictures returned to normal and have remained so after eighteen months' observation.

Clinically the skin lesions were rather suggestive of a generalized lichen scrofulosorum. However, the absence of grouping, the age of the patient, the failure to demonstrate active or healed tuberculosis, the true tuberculous histopathologic architecture, and a lymphatic leukocytosis out of proportion to that of general and cutaneous tuberculosis in our opinion ruled out this diagnosis.

We cannot prove whether the blood picture was the primary pathologic change and the skin expression secondary, or vice versa. In view of the fact that tuberculous structures are found not only in tuberculosis but also in many other infections, when allergic conditions are present, we believe that this case is one of a chronic, low grade, lymphatic leukemia in which the cutaneous eruption is that of a leukamid with a definite tuberculomatous architecture.

515 Grant Street.

ABSTRACT OF DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Transitions between all the various forms of lymphoblastoma can occur. Many cases of lymphatic leukemia, however, remain typically such throughout the course of the disease. The skin manifestations of lymphatic leukemia may be divided into two groups: (1) true leukemic infiltrations of the skin (leukemia cutis) and (2) toxic reactions (leukamids). The authors' case presents certain features of extraordinary interest not only from the clinical but also from the pathologic point of view. The histopathologic features are open to various interpretations concerning which there probably would not be a uniformity of agreement between different pathologists. I believe the case represents a true leukemia cutis in which a tuberculoid reaction is occurring. Sections of the skin revealed numerous tuberculoid nodules, many of them centered about a blood vessel, simulating the microscopic picture of a sarcoid or a tuberculosis cutis indurativa. In several areas, however, the adjacent lymph vessels were packed with lymphocytes and lymphoblasts. There was also a dense infiltrate of immature and mature lymphocytes about arrectores pilorum muscles and also about a sweat duct. This case, therefore, differs from the usual types of leukemia cutis. These may be divided into: (1) the discrete nodular type with or without ulceration; (2) the diffuse erythematous type (malignant erythroderma), and (3) those rare cases in which there are true leukemic infiltrations in and about the blood vessels in the skin with as yet no macroscopic or clinical evidence. I know of only one case of lymphatic leukemia in which a tuberculoid reaction occurred in the skin. Ramozzotti (*Giorn. ital.* **70**:1283, 1929; abstr. *Zentralbl. f. Haut- u. Geschlechtskr.*, April 20, p. 374) describes a typical case of lymphatic leukemia in which there developed lesions which clinically and histologically were papulonecrotic tuberculids and in which the tubercle bacillus was demonstrated. This suggested to the author a tuberculous etiology for both diseases. In the authors' case, however, I believe the more plausible interpretation is that a tuberculoid reaction developed as the result of true leukemic infiltration of the skin, thus simulating the reaction seen in various forms of cutaneous syphilis, in which a tuberculoid reaction is frequently encountered but the etiologic agent is proved to be *Spirochaeta pallida*.

DR. FRED WISE, New York: The authors' case is one of extreme interest, both from the clinical and from the histologic aspects. It demonstrates better than any case I have seen for a long time the futility, in certain instances, of trying to base a diagnosis on clinical grounds alone, no matter how expert a clinician the physician may be. I am sure that any one who sees a picture of this type would be unlikely to recognize the condition on clinical grounds. I should like to ask whether guinea-pig inoculations and tuberculin tests were performed, and whether there is any relationship between this picture and the famous case reported by Bruusgaard in which he was able to demonstrate tubercle tissue in biopsies from almost any area of the involved integument.

DR. GEORGE J. BUSMAN, Pittsburgh: As to whether or not this lesion may be due to two entities, it may be. At first we thought of a generalized lichen scrofulosorum, but the case is unique in that the blood picture has remained normal for several months and the lesions have dissolved. If this is leukemia, it is a question of what effect the spleen extract had. We are trying it in other cases. Guinea-pig inoculations and sections stained for tubercle bacilli were negative.

OUR EIGHTEENTH CENTURY METHOD OF TREATING SUPPURATIVE OTITIS MEDIA

A CRITICISM AND A REMEDY *

JOHN A. PRATT, M.D.
MINNEAPOLIS

In the past and present methods of treating suppurative otitis media, the most important factor, drainage, seems to have been ignored.

The first principle in surgery has always been, "Where pus is present, evacuate and establish drainage." In suppurative otitis media, if nature has not ruptured the drum, it is incised; but few follow up the next step and encourage continuous drainage. It is this one important step of continuous drainage on which success or failure depends.

If it were possible to drain a suppurating middle ear, attic, antrum and the mastoid cells through the eustachian tube, mastoidectomies would be very rarely performed. When the eustachian pathway is not sufficient, drainage must be established through the drum or the mastoid bone.

Following this thought of continuous drainage, a review was made of thirty-nine books dealing with diseases of the ear, published from the year 1888 until 1929. Only three of these books suggested frequent changing of cotton in the ear canal and not one of them described the method of application. Twenty of them spoke of irrigations only. Four recommended irrigations with drying of the canal. Nine gave irrigations with drying and a gauze pack for the first twenty-four hours. Three ignored any line of cleansing.

From 1911 to 1929, only three papers on suppurative otitis media were read in the American Academy meetings and only one in the meetings of the American Medical Association. Of the eleven discussions on a paper by Dr. Wolfe in 1923, mine was the only one mentioning continuous drainage.

Until Dr. M. C. Fox wrote a paper in 1929, there had been no reference made to the use of continuous drainage in suppurative otitis media since 1906; at least I have been unable to find any.

In a review of 192 papers written on middle ear diseases, published in the eye, ear, nose and throat year books from 1906 to 1929, 152 papers were negative in reference to ear cleansing. Twenty-five recommended irrigations; 6, from one to many dryings; 3, irrigations

* Read before the Section on Laryngology, Otology and Rhinology at the Eighty-First Annual Session of the American Medical Association, Detroit, June 26, 1930.

with gauze pack for the first twenty-four hours; 3, twenty-four hour gauze packs only; 2, aspirations; 1, gravity drainage.

This is not a criticism of any of the innumerable methods of treatment but of the method of drainage used after pus begins to flow into the external auditory canal.

If some still believe that medicine can be dropped into a pus-filled middle ear cavity, they should do it but should also use drainage. Continuous drainage does not interfere with any line of treatment.

The powerful suction of capillary attraction is well known. It is the use of this well known force that is employed in the dry treatment of suppurative otitis media. With a well made, elongated swab of highly absorbent cotton, all fluids in continuity can be drained. In following this fact, I have been using continuous drainage of the middle ear for the past twenty-five years, with what I consider remarkable success.

Starting January 6 of this year, at Houston, Texas, and ending March 25 at Vancouver, B. C., I attended ten meetings of eye, ear, nose and throat societies, and met hundreds of men doing special work, and yet found only two using the method of continuous drainage in suppurative otitis media, one of these being a former student of mine at the University of Minnesota.

METHOD OF TREATMENT

To make the swabs for the dry treatment of suppurative otitis media, the following method is used:

1. A small piece of absorbent cotton is laid on the tip of the first finger of the left hand; then the end of an applicator (or toothpick) is placed in the center of the cotton.

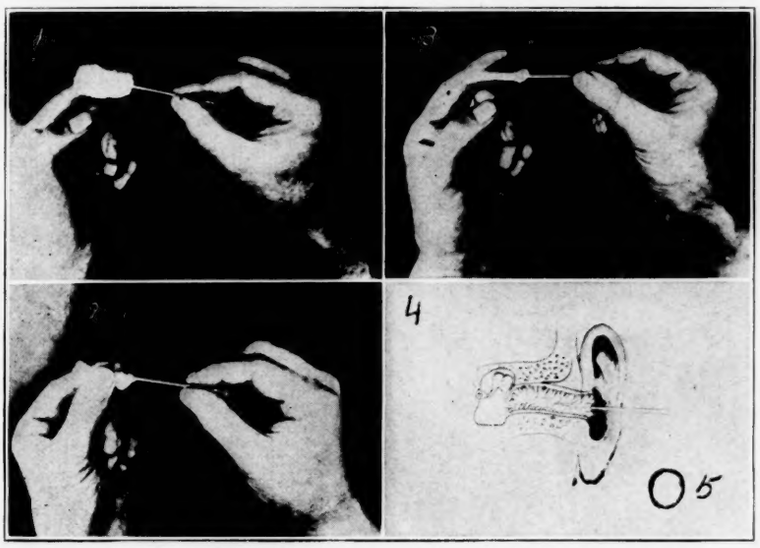
2. The thumb is placed lightly over the cotton and applicator (or toothpick); then with the right hand, the applicator is twirled away from one, leaving a small space between the thumb and the first finger to shape the cotton.

3. The cotton is now an evenly wound swab, about 1½ inches long.

4. The swab on the applicator is now inserted in the ear canal down to the drum and the discharge wiped out. When the canal is dry, a swab is left in the canal and this *must touch the drum*. To remove the applicator, one finger is placed on the cotton, the applicator is slightly turned in the opposite direction to loosen it, and then it is withdrawn.

5. The swab must be made small enough to pass through a medium sized ear speculum.

6. The swab should be changed as often as it is half filled with discharge, whether five minutes or five hours, the object being to suck the discharge out of the middle ear cavity as rapidly as it is formed.



The method of making swabs for the dry treatment of discharging ears. The numbers correspond to steps in the method; 5 is the size of the hole through which the swab should pass.

The pain present in suppurative otitis media is due to the pressure of the discharge confined in the middle ear and antrum of the mastoid. With the dry treatment, one is able to remove the pus and so relieve the pressure pain. With the patient in the office for an hour, one can determine the proper outline for the treatment of the case.

It will be found necessary in acute cases to change the swabs night and day for the first forty-eight hours. The reward is a rapid recovery, free from pain, the reduction of the septic condition and avoidance of mastoiditis.

There is no doubt that the use of dry treatment and proper mastoidectomies in acute suppurative otitis media would banish chronic suppurative otitis media.

The reaction of the discharge and of the patient to the treatment is an indication of when and when not to perform a mastoidectomy.

The one objection given to this method of treatment is the time it takes to instruct the patient. It is rarely necessary to instruct the patient after the second day. I have a printed card that illustrates and describes the method of making and applying the swab. This card is given to the patient.

While in Los Angeles this winter, I spent every morning for two weeks instructing the interns and nurses and treating the patients in the outpatient department of the County General Hospital by this method. The results of the first week's treatments were so satisfactory that the method was adopted for the hospital by the eye, ear, nose and throat staff.

1753 Medical Arts Building.

ABSTRACT OF DISCUSSION

DR. AUSTIN A. HAYDEN, Chicago: The statements that Dr. Pratt makes in his paper are startling. They certainly are to me. He contemplates what I regard as continuous suction, or capillary action, through a cotton plug rather loosely fitted into the external auditory canal, and often done by the patient himself. Based on an experience, as I understand, of twenty-five years, and having treated a considerable number of cases in that time, he states that the pain is promptly relieved, suppuration is dried up, and chronicity is prevented. It seems to me that is a large order. It is a statement that I think will arouse a good deal of doubt in the minds of a great many men here. The author's thesis is clear, his argument is lucid, and the paper admits of little discussion as I see it. The answer must be to try it for oneself. We have the word of an experienced otolaryngologist backed by wide experience with these cases to the effect that startling results have been obtained through a method that perhaps we have not used, at least according to the definite technic that he has followed. I might say that I doubt whether Dr. Pratt's results will be repeated by other men, but if they are a long step forward has been accomplished by this paper in the treatment of ear suppuration. If these results are not obtained by some of us when we return

home we shall have to conclude that we have listened today simply to an interesting and enthusiastic report of clinical observations which we ourselves after a fair trial have been unable to reproduce.

DR. DON M. CAMPBELL, Detroit: One must admit at once that the ideal of perfect surgical drainage after incision or spontaneous rupture of the tympanic membrane in acute suppurative otitis media is most desirable, and one would like to agree with the author that the proper management of acute middle ear conditions and proper mastoidectomy in acute suppurative otitis media would banish chronic suppurative otitis media. However, the carrying out of such a program is not without some difficulty, for the following reasons: First, the natural timidity of people about putting anything smaller than their elbow in the ear will be found to be a deterrent to the following out of the directions in the introduction of the drain in home treatment for both cleansing and drainage. Second, the frequent introduction of the cotton applicator into the external auditory canal, down to and in contact with the drum membrane, in many cases will be found to be quite disagreeable, if not painful. On account of the extra sensitiveness of the canal and the inflamed tympanic structures this will no doubt militate somewhat against the exact carrying out of the directions by the patient in the home treatment. Third, there might be something said about the possibility of introduction of secondary infection by the continuous application of cotton-covered applicators, for though they may start sterile they might easily become infected before they reach the auditory canal and drum. Fourth, the treatment, if carried out in the office, is a time-consuming method which, of course, should not be allowed to interfere with the carrying out of such a treatment, if it can be shown that the result to the patient justifies the expenditure of time. From the surgical standpoint the use of an ideal form of drainage in the management of middle ear and mastoid diseases is highly desirable.

DR. JOHN F. BARNHILL, Indianapolis: Adequate drainage of suppurating cavities is one of the oldest and most valuable principles of surgery. Any plan whereby free, continuous drainage from a discharging middle ear is secured is an accepted principle in otology, for unobstructed exit of the aural discharge is essential to prevent pain, hasten restoration of the infected tissue to normal, and prevent extension of the disease to adjacent structures. The author speaks of lack of proper directions in textbooks concerning methods of draining discharging ears. I feel that his statement in this respect can scarcely be justified by facts, since most modern textbooks are full and explicit on this point. In my publications on the subject I have not only described the necessity for drainage sufficiently but have in addition illustrated the methods of incision very fully. Concerning the use of the cotton cylinders as the best means of securing continuous drainage, I should have some fear that the patient in the process of inserting these with his own hands might infect them and thus reinfect the middle ear and prolong the discharge. The laity, even when instructed, seldom give strict attention to antiseptic procedures when treating themselves. I cannnot agree with the statement that any known plan of treating an acute discharging ear will positively insure the patient against complications. Free drainage will usually do this, but there are instances of acute aural infection, as that following scarlet fever, in which the character of the pathogenic organism is such that complication takes place almost from the beginning, and all efforts fail to check the progress.

DR. FRANCIS V. GOWEN, Philadelphia: During the acute stage I make a wide incision into the drum membrane and keep it open by irrigation, reincising as often as is necessary. Since the infection reaches the ear from the nasopharynx by way of the eustachian tube, a shrinking solution is dropped into the nostrils, aerating the nasopharynx, as advised by Coates, followed in five minutes by an antiseptic solution. This treatment eliminates the ideal culture mediums of the nasopharynx, viz., darkness, moisture, food and heat, destroys the bacteria in situ, and also promotes eustachian drainage. After the acute stage, prophylactic measures are instituted, adenoids and diseased tonsils are removed, and submucous resection and middle ear turbinectomy are done, if indicated. Necessary and conservative treatment as advised by Skillern is applied to the lower turbinates. Any other conditions supplying food for bacteria or preventing proper aeration of the nose and nasopharynx are remedied.

DR. LYMAN RICHARDS, Boston: Those who are called on to deal with these conditions in the average outpatient clinic must devise some form of treatment that can be carried out at home. The time cannot be spent with these patients that physicians do in the office. Consequently, parents must be instructed as to any local treatment that seems feasible. One of the difficulties encountered has been mentioned by Dr. Campbell, matters of great reluctance on the part of parents to insert any cleansing object to the proper depth in the auditory canal. This difficulty has led me to adopt the use of a special short meshed wick, manufactured originally as a remnant from a twine mill, which, having a high capillary reaction like a lamp wick, tends to facilitate drainage from the needle here. Once properly inserted into the canal it needs changing only at intervals of forty-eight hours or more, for which procedure the child can return to the outpatient clinic. In the meantime a small piece of cotton placed on the outside where the wick comes out of the external auditory meatus can be frequently changed by the parent, thus promoting free drainage and at the same time maintaining cleanliness and comfort. This wick is efficacious principally and the discharge is serosanguineous. When it becomes purulent, the wick tends to float out with the discharge, and some form of irrigation will prove more efficacious.

DR. HAROLD M. HAYS, New York: One of the chief things to be considered in infections of the middle ear is the amount of drainage, and repeated observations should be made to see whether the original incision in the drum is sufficiently large for drainage. If the discharge from the ear canal is profuse, it is not necessary to insert anything into the canal to increase the discharge. All such cases should be under daily observation, preferably in the office if the patient is ambulatory, so that careful examination with an otoscope can be made in order to note the condition of the incision and particularly to note whether there is pulsation. All know that it makes little difference how large the original incision is, for within twenty-four hours most of it closes up. Rather than performing multiple incisions in the drum, one can keep the original incision open by inserting an electrical otoscope tightly into the ear canal and sucking in and out through a piece of tubing attached to the otoscope. There are certain adjuvants to treatment that are more than worth while. A small child can be placed in front of an irridescent lamp, or such a lamp can be suspended over a crib for an hour or so at a time. Patients coming into the office can be treated by inserting a small wick of cotton immersed in a mentholated solution into the ear canal and having such patients sit in front of an infra-red lamp. I shall be most happy to try Dr. Pratt's treatment in the office but can hardly feel that a lay person can be properly instructed to use it at home.

DR. EMIL AMBERG, Detroit: I think Dr. Pratt's treatment, under certain circumstances, is excellent, and, like the last speaker, I would commend it, but not in the office. That is the point to which I would object in acutely infected ears. I think that a patient with such an ear should be in bed and has no business to come to the office. If the eardrum is incised and the patient put to bed, the results will be much better and there will be fewer complications. I also deprecate the introduction of irritating substances into the acutely inflamed ear after incision. The patient should have a rest, nature should be given a chance, and insult should not be added to injury. Therefore, I urge that these patients be sent home and not allowed to come to the office every day, but kept in bed and watched.

DR. J. A. PRATT, Minneapolis: If the treatment is tried as I have described it I think it will be adopted. The people must be educated; I showed that they can be in Los Angeles last winter. In reference to the aseptic part, the patient is instructed to wash his hands, that is all. If others are doing it for the patient, they are simply told to wash their hands and keep clean. If care had to be taken about every germ that came along, no

one would eat or sleep in a month. But one can keep away from terrific infection. Work in the dispensary has shown that the results are marvelous. The paper was not dogmatic. I did not say there would not be chronic suppurating ears or mastoidectomies or anything of that kind. I said that if this was done there would be less likelihood of chronically affected ears; and in my opinion they will not occur because it is the infectious material that is allowed to stay there that brings on the chronic case. This has been used in all the ear cases at the state university and dispensary, and the results are marvelous. I may be considered radical, but one who had seen the hundreds of cases that I have would think differently about it. All I ask is that it be given a trial.

Clinical Notes, Suggestions and New Instruments

POLYCYSTIC KIDNEYS WITH BILATERAL NEPHROLITHIASIS *

ALEXANDER HAMILTON PEACOCK, M.D.
AND
DONALD G. CORBETT, M.D.
SEATTLE

Polycystic kidneys are always spectacular, on account of their unusual size, the fact that nine out of ten are bilateral, and the limitations of surgery that can be safely employed.

The occurrence of calculi in this type of kidney is scarcely mentioned in the literature. Thomas [1] reported a case of staghorn calculus in a kidney presenting multiple cysts but not polycystic. In discussing this case, Greene [2] stated that he saw a case of staghorn calculus in a polycystic kidney; no operation was done. He quoted Sieber as also having seen 8 cases of calculi in 220 polycystic cases and Braasch as having seen 4 calculi in 31 cases of polycystic disease.

Young [3] states that polycystic kidney may be the site of practically any other renal disease, as calculus, hydronephrosis, pyelonephritis or tuberculosis.

Surgery on polycystic kidneys has always carried a high rate of mortality. Brin [4] reported a mortality of 31.8 per cent in twenty-two cases of nephrotomy. Nephrectomy carries a still greater death rate.

A case of multiple bilateral calculi in polycystic kidney with successful operation was thought to be of sufficient interest to report.

REPORT OF CASE

History.—A man, aged 45, born in Nebraska, now operating a fox farm in Alaska, referred by Dr. Thomas B. Rhone of Petersburg, Alaska, was admitted to the Providence Hospital, Seattle, April 10, 1929. The patient's father died at the age of 56 of cardiorenal disease; his mother at 70 was living and well. He had two brothers living, both of whom had kidney disease, and three sisters, of whom he knew little. The patient had had the diseases of childhood. In 1900 he sustained a fracture of the left humerus and in 1913 a fractured jaw. One year before admittance, after thirty-six hours of a right renal colic, the patient passed a calculus. This was accompanied by hematuria. Three months later, another calculus escaped from the right kidney. A dull ache had been almost constant in the right upper part of the abdomen and back, occasionally radiating into the right groin. There had been no pain in the left side. Blood had been observed in the urine intermittently, sometimes a considerable quantity of it but no clots. The urine had been cloudy for several years. On standing, considerable sediment was thrown down. The urine had a strong ammoniacal odor. The patient had felt tired out and weak on exertion. He had lost weight and had little pleasure in eating. He had no gastric pains but suffered with gas after a heavy meal.

Examination.—The patient was 5 feet 9 inches (175 cm.) tall and weighed 161 pounds (73 Kg.). His temperature was 98.2 F.; pulse, 80; respiration, 18 at noon; blood pressure, systolic 160, diastolic 100. The blood Wassermann reaction was negative. Chemical examination of the blood revealed: urea nitrogen, 30 mg.; creatinine, 1.9 mg. The blood count revealed: hemoglobin, 62 per cent; erythrocytes, 3,560,000, and leukocytes, 19,050. A phenolsulphonphthalein test returned 27 per cent in the first hour and 20 per cent in the second.

The teeth were in poor condition with infected gums and many teeth were decayed. The abdomen relaxed easily. Both kidneys were easily palpable; the lower poles were below the crest of the ilium. Percussion over the right kidney produced pain.

The bladder was irritable, with a capacity of 120 cc. The urine was cloudy with a specific gravity 1.010, albumin plus, indican and sugar negative. Microscopically there were many pus cells and staphylococci; no tubercle bacilli were found. The ureters were easily catheterized, with obstruction noted near the right renal pelvis. The right kidney urine was milky in appearance and contained many staphylococci. The left kidney urine was almost clear and contained only a few staphylococci.

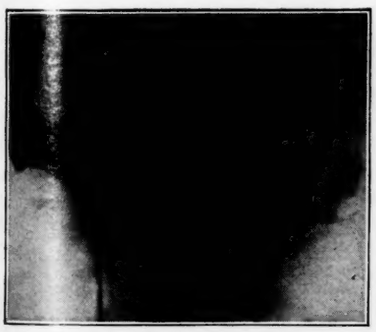


Fig. 1.—Multiple calculi in polycystic kidney.

Fig. 2.—Double pyelogram of polycystic kidney containing bilateral calculi.

Fig. 3.—Control, Oct. 12, 1929, after removal of calculi from right kidney, showing calculi in left kidney.

The control roentgenogram (fig. 1) showed a shadow in the upper right part of the abdomen which measured 3 inches long and 1½ inches wide (7.5 by 4 cm.). Above this was another shadow, ¾ inch in diameter. The left side showed a mass composed of several small, apparently faceted shadows, the whole mass being about 2 inches in length and ¾ inch in width.

The injected film (fig. 2) showed several large collections of opaque medium on the right side, one of which was superimposed on the previously described shadow, and the others surrounding it on all sides. The left side showed a greatly dilated and widely separated superior and inferior calix surrounding the previous collection of shadows mentioned.

The condition was diagnosed as polycystic kidneys with multiple bilateral calculi.

* From the Urological Department, Providence Hospital.

1. Thomas, B. A.: Urol. **20**: 451 (Oct.) 1928.
2. Greene: J. Urol. **20**: 445 (Oct.) 1928.
3. Young, H. H., and Davis, D. M.: Practice of Urology, Philadelphia, W. B. Saunders Company **2**: 25, 1926.
4. Brin: Encyclopédie française d'urologie, 1914, 11,

First Operation.—April 20, under ethylene gas anesthesia, an oblique incision over the right ilium was made to give a good extraperitoneal exposure of the kidney. The latter was delivered and measured 30 by 13 by 12 cm. The surface was entirely covered with clear cysts from a pinhead in size up to 4 cm. in diameter. Several were punctured and contained pale, clear fluid. The pelvis was exposed posteriorly and the calculi were easily palpated. These were held between the fingers and cut down on. The stones were soft and had to be scooped out. The calices were easily explored with the finger. A drainage tube (24 French) was placed in the pelvis and a purse-string suture used. The wound was closed in layers.

The first night the right kidney drained 720 cc. of urine. The patient left the hospital on the twenty-first day with the wound healed, the blood pressure 130 systolic and 90 diastolic, and the weight 159 pounds (72 Kg.). The patient returned to Alaska and felt well for two months, when he began to have colic in the left side and back. These attacks were periodic and were apparently brought on by physical effort. Oct. 10, 1929, he returned to Seattle for the second operation.

Second Operation.—October 14, again with ethylene gas, the left kidney was exposed in the same manner as the right one had been six months before. The kidney was higher under the costal margin, necessitating the resection of the eleventh rib to deliver the organ. A similar picture of cysts was seen, blue, yellow and slate colored, all of different sizes (fig. 4). The ureter was isolated and the pelvis opened posteriorly. Through this incision were expressed several soft calculi and a quantity of putty-like substance. When the uppermost calculi were released, a quantity of white, creamy pus escaped. A rubber drain in the pelvis was secured with a purse-string suture. The kidney was replaced and the wound repaired.

Convalescence was placid. The patient was discharged on the twenty-fourth day; his weight was 148 pounds (67 Kg.). Feb. 1, 1930, he wrote that his weight was 165 pounds (74.8 Kg.), that the urine was at times hazy, and that he felt fine.

SUMMARY

1. Multiple calculi in bilateral polycystic kidney are exceedingly rare.

2. Surgery of the polycystic kidney should be unusually conservative.

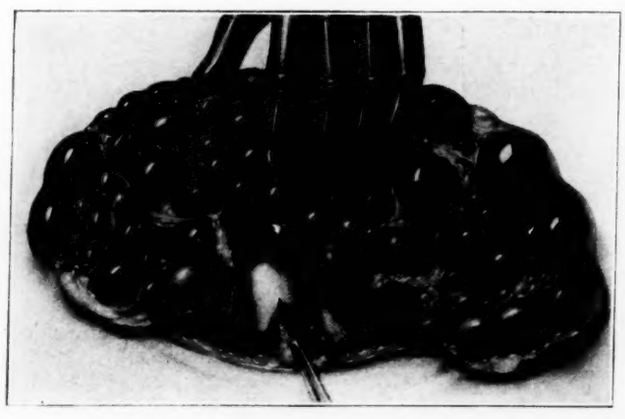


Fig. 4.—Appearance of cysts from left kidney; actual length, 11 inches (28 cm.).

3. Chronic staphylococcus infection of the urinary tract ends, frequently, in the formation of calculi.

340 Stimson Building—1215 Fourth Avenue.

The Control of Nature.—Human progress has been a series of triumphs over natural forces. But when anything new is proposed, certain people cry out that this is a perversion of nature. Of course it is. Man rules by bending the world to his will and to the service of his ends. Man has progressed by mastery over other forces.—Cowdry, E. V.: Human Biology and Racial Welfare, New York, Paul B. Hoeber, Inc., 1930.

A CASE OF OSTEOGENESIS IMPERFECTA INFANTILIS

JOHN INGLIS, A.M., M.D., DENVER

The mother of this child was 26 years of age. She was one of a family of eleven, all of whom were living except one child who died at 2 weeks of age of smallpox (the mother having contracted it) and one who died during the influenza epidemic of 1918. She weighed 152 pounds (69 Kg.) and was strong, healthy and well nourished. Her past history was entirely negative. The father was 24 and belonged to a family of four boys. He weighed 156 pounds (71 Kg.) and had always been well and strong. The Wassermann reaction was negative in both parents.

Fig. 1.—Osteogenesis imperfecta: 69 skeletal fractures, as follows: 32 costal; 20 costocartilaginous separations; 17 fractures of the extremities; comminuted eggshell fracture of skull; scapulae and pelvis poorly developed.

The pregnancy was normal in every way. The mother went into labor about 10 a. m., with pains every twenty or thirty minutes. These pains continued irregularly until 3 or 4 p. m., when they subsided to begin again at about 7:30. They then continued until the birth of the child by podalic extraction at 2:30 a. m. Breech presentation occurred, with the thighs more or less at right angles to the body.

Great difficulty was experienced in the extraction of the child. When the legs were brought down, crepitus was felt over both the legs and the thighs. When the body was extracted, crepitus was felt over all the ribs. The greatest difficulty was found in getting the after-coming head. Dr. Evans, who was making some pressure above the pubis, remarked that he could not feel the head at all. After the head was finally extracted, it was found to be practically without a skull. This accounted for the difficulty in delivery, the usual methods only causing the head to enlarge parietally.

The child lived only a few minutes. A roentgenogram of the body showed seventy-four distinct fractures which had made an effort to unite again in the uterus.

REPORT FROM X-RAY LABORATORY

The roentgenologist reported that the condition was periosteal dysplasia. He found thirty-two rib fractures, twenty costovertebral arthrophymas, seventeen fractures of the extremities and many fractures (eggshell) of the skull. The bones of the skull, the scapulae and the pelvis were poorly developed. The spinal segments were normal.

CASES IN THE LITERATURE

This condition has been given a great variety of names. It was formerly thought to be intra-uterine rickets. This theory has been given up.

Chaumier of France reported a case in which there were 113 fractures. Most of these patients die at birth. Chaumier's patient lived thirteen days. It was delivered by a midwife.

Labor came on three weeks before term. It was a head presentation, and the baby weighed 3 pounds (1.4 Kg.).

De Paul reported a case in 1851. At that time he doubted the rickets theory.

Kassowitz of Germany reported one case. He leaned to the idea of intra-uterine rickets.

Rivière reported one case in 1911. This baby lived twelve days. Rivière thought it was syphilitic.

Getsava reported a case in 1913. As in all the others reported, the baby died.

AUTOPSY REPORT

The autopsy was performed on the body of a full term, white male infant measuring 41 cm. long and weighing 6 pounds and 12 ounces (3 Kg.).

A crescentic incision extended over the right clavicle.

There was a large amount of brown hair on the scalp. The head felt like a sac filled with fluid. Small bony plaques were in the area of the cranial bones.

There was a moderate amount of lanugo hair over the extremities. The pupils were equally dilated. The ears, nose and mouth appeared normal. There was a distinct feeling of crepitus on the midtrabecular line on both sides of the chest. The cord had dried.

There was a moderate amount of edema in the scrotum.

Crepitus was felt in both humeri, both forearms, over each femur and along the extent of the fibula. There was a slight amount of edema in the legs and feet.

The length of the right arm was 14 cm.; of the left arm, 14 cm.; of the right thigh, 4 cm. (measurement taken from the tip of the inguinal fold to the knee); of the left thigh, 4 cm. (measurement taken as for the right). The lower extremities measured 14 cm. from the tip of the toe to the upper portion of the inguinal canal.

Fig. 2.—Spinal segments normal.

In the abdominal cavity the position of the organs was normal. The small and large intestines were normal with little meconium present.

The pancreas weighed 2 Gm.

The liver weighed 97 Gm. It was normal in shape and size. The capsule was normal. The cut surface was also normal. The right and left suprarenal glands each weighed 3 Gm. and appeared normal. The kidneys each weighed 10 Gm. and appeared normal.

The gallbladder was normal.

The spleen was normal in shape, being as broad as it was long, with a deep notch on the anterior border. The capsule was normal. The cut surface was also normal. It weighed 8 Gm.

The thymus measured 6 by 4.5 by 1.5 cm. and weighed 12.5 Gm. The thyroid was not cystic and appeared normal.

The mesenteric glands were numerous and prominent. Otherwise the abdominal organs appeared normal. The omentum was normal.

The right and left pleural cavities and pericardial sac contained a large amount of fluid (probably embalming fluid and not hemorrhagic fluid).

The right lung weighed 16 Gm., and the left 14 Gm. Both appeared normal, as did the heart.

Along the spine was a diffuse traumatic hemorrhage with a separation between the fourth and fifth dorsal.

In the brain there was a diffuse traumatic hemorrhage around the occipital and temporal lobes above the tentorium cerebri and the cerebellum.

Fig. 3.—Faulty development of bones of pelvis; fractures of the extremities.

836 Republic Building.

A MOTORLESS OXYGEN THERAPY APPARATUS *

RUSSELL L. CECIL, M.D., AND NORMAN PLUMMER, M.D.
NEW YORK

The value of oxygen therapy in the treatment of disease has been demonstrated in the last decade by the accumulation of extensive clinical and experimental evidence. A continuous supply of from 40 to 60 per cent oxygen has been found to be most beneficial. Administration with the funnel or the nasal catheter does not supply this optimal concentration to the lungs. The mask has been given an extensive trial but has been found unsatisfactory for continuous therapy. The oxygen chambers, as developed by Haldane,[1] Barcroft,[2] Stadie,[3] Binger,[4] Barach,[5] and others, are satisfactory but they are expensive to operate and available only to a few hospital patients.

Leonard Hill[6] recognized the importance of constructing a portable oxygen therapy apparatus that would have the advantages of continuous flow and high concentration. In 1921 he described a bed tent that satisfied certain of these requirements but that was cumbersome to move and inefficient to operate.

* From the Second Medical (Cornell) Division of Bellevue Hospital, and the Department of Medicine, Cornell University Medical College.

1. Haldane, J. S.: Brit. M. J. **1**: 181 (Feb. 10) 1917.
2. Barcroft, J. H.; Hunt, G. H., and Dufton, D.: Quart. J. Med. **13**: 179 (Jan.) 1920.
3. Stadie, W. C.: J. Exper. Med. **35**: 337 (March) 1922.
4. Binger, C. A. L.: Mod. Hosp. **24**: 186 (Feb.) 1925.
5. Barach, A. L.: J. Clin. Investigation **2**: 463 (Aug.) 1926.
6. Hill, Leonard: Proc. Physiol. Soc. **1**: 20, 1921.

This apparatus was modified considerably by Barach and Binger,[7] but the same disadvantages remained.

In 1926 Alvan Barach[8] described a new apparatus that was definitely more satisfactory. He incorporated the head tent idea of Roth,[9] which made it much less cumbersome. The ventilation was obtained by a small motor and fan; the air was cooled and dried by passage through cracked ice, and the carbon dioxide was eliminated by passage through soda lime. This portable therapy apparatus is the one most commonly used at the present time. However, it still presents certain mechanical difficulties, which are particularly those that have to do with the motor and the cooling system. The motor causes a certain amount of noise, is apt to stop suddenly, is dependent on an electrical connection and requires lubricating oil, which is considered dangerous when used near high pressure oxygen. The cooling system requires much attention in order to keep it filled with ice, and the leakage of water causes considerable inconvenience. In an attempt to overcome these disadvantages, the apparatus reported here has been developed.

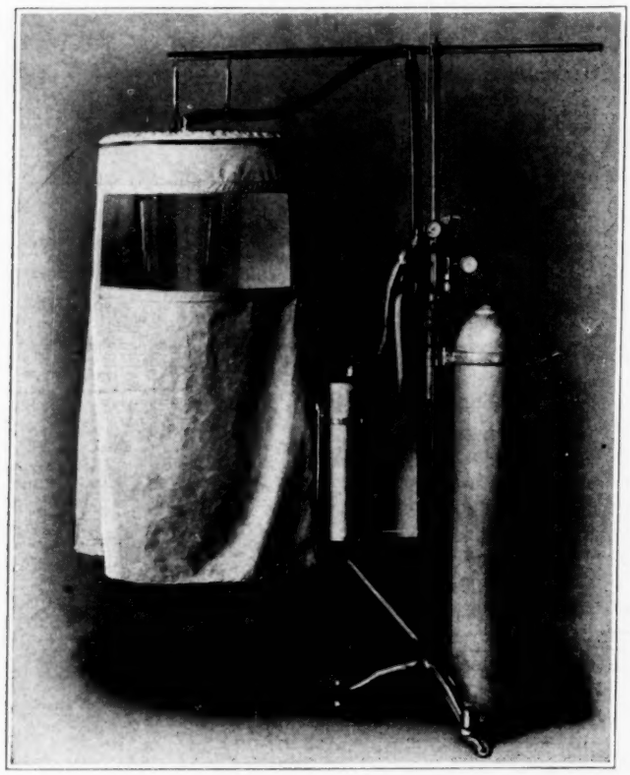


Fig. 1.—Motorless oxygen therapy apparatus, showing hood, operating mechanism and supports.

The motor blower is replaced by an injector, designed by the American Atmos Corporation. It utilizes the high pressure flow of oxygen for its motive power, drawing the air from the hood through the regenerator on the one side, and forcing it through the cooling system and back into the hood on the other. The injector may be regulated to furnish as much or as little circulation as is suitable. In this particular apparatus it is set to give an air exchange of 100 liters a minute.

The minimum oxygen requirement for this type of apparatus has been found to be approximately 5 liters a minute. For simplicity, the injector is set to use this minimum amount, which furnishes an atmosphere of about 50 per cent oxygen concentration to the patient. If a higher percentage of oxygen is required, it may be added through an auxiliary reducing valve. A gage connected to this valve registers the flow of oxygen in liters per minute. Another gage on the injector gives the pressure of oxygen in the cylinder. At the beginning of the treatment it is desirable to obtain the optimum oxygen concentration in the hood as quickly as possible. This is done by pressing a button on the front of the apparatus, which releases a quantity of oxygen and which will increase the oxygen percentage in the hood to 50 per cent in two minutes.

The carbon dioxide is removed from the air by passage through a regenerator of soda lime. This reduces the carbon dioxide in the air entering the hood to less than 0.5 per cent. The regenerator contains a sufficient amount of soda lime for more than twenty-four hours of treatment. Two types of regenerators have been used, one refillable and the other sealed. For the usual hospital practice, the refillable type is almost as handy and more economical. The sealed type is convenient when loose soda lime is not readily obtainable.

In the cooling system an attempt has been made to avoid the inconvenience of the use of ice and at the same time to produce, if possible, even greater cooling of the air. The system has been adapted to the use of "dry ice" (carbon dioxide snow), and all tests made up to the present time have proved very satisfactory. The air coming from the injector passes through the cooler, the inner walls of which form a container of the proper size to hold a 40 pound cube of "dry ice." The outer walls are double and lined with felt to afford insulation from the outside air. A water trap with a valve is placed at the lowest level of the circulatory system in order to remove the moisture that condenses from the expired air. A valve is also inserted at the bottom of the metal container to allow for the drainage of water when it is more convenient to use ice, or salt and ice. It has been found that a cake of "dry ice" will last from twenty-four to thirty-six hours. Ice and salt must be renewed every eight to ten hours.

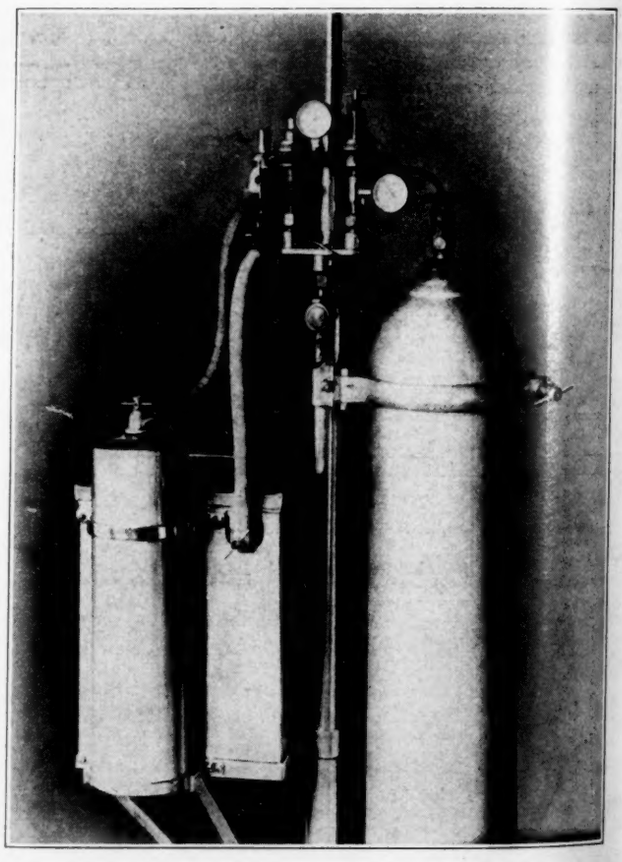


Fig. 2.—Operating mechanism of motorless oxygen therapy apparatus, showing regenerator, cooling system, injector, high pressure valve, by-pass valve, gages and oxygen tank.

The air from the cooling system passes directly into the side of the hood through a short piece of rubber tubing. This modification from the usual method of carrying the tubing to the top of the standard and thence into the top of the hood has been found to be a great improvement over the old arrangement. By this method the heating of the air by radiation from the metallic parts of the apparatus and from the room is largely

7. Barach, A. L., and Binger, C. A. L.: Portable Oxygen Tent, J. A. M. A. **85**: 190 (July 18) 1925.
8. Barach, A. L.: New Oxygen Tent, J. A. M. A. **87**: 1213 (Oct. 9) 1926.
9. Roth, P.: Bull. Battle Creek Sanitar. & Hosp. Clin. **19**: 178, 1924.

prevented. With a room temperature of 73 F., the temperature of the air entering the hood was 22 F. when "dry ice" was used and 43 F. when ice and salt was the cooling substance. The air in the hood is warmer than the air entering the hood but cooler than the air of the room. At no time has a patient complained of the air being too cold.

The hood is of the circular type as described by Roth. It is 54 inches long and 26 inches in diameter, made of a heavy rubberized material, provided with a large window and supported from the top by a conical piece of metal. The standard and cross rod are adjustable, and the hood is hung from two small springs which make the apparatus flexible and easy to manipulate. The pedestal is of substantial construction with rubber-tired casters. The oxygen cylinder is easily mounted without being lifted. The entire outfit is easily moved from one place to another as a single unit.

The operation of the apparatus is extremely simple. With the oxygen cylinder in place, the regenerator attached and the "dry ice" or ice in the cooling chamber, it requires merely the turning of the valve on the oxygen cylinder to obtain approximately 50 per cent of oxygen in the hood. This percentage may be obtained rapidly by pressing the button on the front of the apparatus, or, with the outfit running, the oxygen may be increased by turning a valve. The oxygen cylinder is renewed every twelve hours, and the soda lime and "dry ice" every twenty-four hours, or, if ice and salt are used, it is supplied every eight hours.

The portable oxygen therapy apparatus that is described here has definite advantages which may be enumerated as follows:

1. Simplicity, and therefore very slight probability of the mechanism stopping suddenly or getting out of order.
2. Elimination of the use of a motor blower, thereby avoiding (1) the noise; (2) the hazards caused by sparks from the motor and by the use of oil near high pressure oxygen; (3) the attention which a motor requires, and (4) the necessity of locating the apparatus near an electrical connection.
3. A more efficient cooling system, with the use of "dry ice" instead of ice. This eliminates the necessity of frequent drainage of the cooling system and of renewing the cracked ice every two to three hours.
4. The apparatus is easily manipulated and is designed to give efficient oxygen treatment more comfortably and more economically to the sick patient.

A CASE OF ACONITINE POISONING CAUSING CARDIAC COLLAPSE

EDWARD F. HARTUNG, M.D., NEW YORK

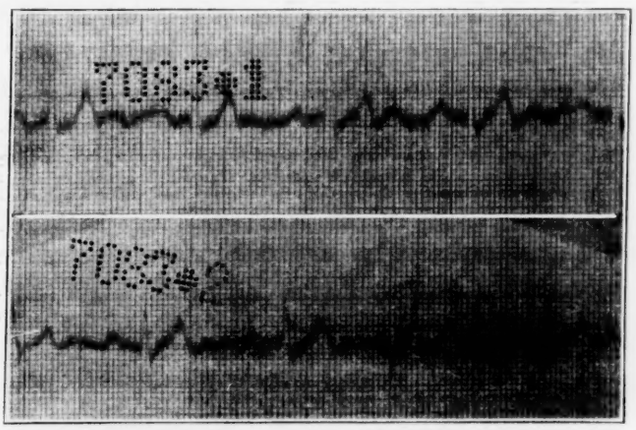
This case of aconitine poisoning is reported primarily to acquaint physicians with the possibility of its unsuspected occurrence. There are probably other cases of mild and severe aconitine poisoning throughout the United States which are being overlooked. Aconitine is a drug that finds little usefulness nowadays and naturally does not enter the physician's mind. Records of aconitine poisoning in any form are unusual in modern medical literature. In my perusal of the literature back to 1883, I could find only three case reports of aconitine poisoning in man with specific mention of its effect on the heart. There were no recent cases. Also, this is apparently the only case in man in which electrocardiographic records were obtained.

REPORT OF CASE

E. O., a merchant, aged 31, weighing about 242 pounds (110 Kg.), drank at about 4 p. m. a small amount of whisky which he had purchased a few weeks before on a steamer bound for New York. The estimated quantity taken was probably less than 3 drachms (11 cc.). The patient rarely used alcohol in any form. At first he felt exhilarated and took a long walk, but in a half hour he felt depressed and was unusually silent. He had a light dinner and then went to a theater. While in the theater about 9:30 he began to have difficulty in breathing and became quite faint, dizzy and weak. He said he felt that he was dying. He began to perspire profusely and his companion noticed that his skin was cold, white and clammy. He was given some spirit of ammonia but this failed to relieve him. Positive collapse lasted for two hours until he arrived home and was put to bed. He passed a rather uneventful night. He did not vomit or have diarrhea or any of the classic signs of aconitine poisoning, such as tingling in the mouth, stomach and skin. He did complain of moderate salivation. The outstanding factors were a great general depression and marked anxiety.

He was seen by me the following morning, and his chief complaint at that time was weakness and a feeling of faintness and uneasiness over the precordium. On examination he was outwardly normal except for the fact that he was pale and his skin was cold. His breathing was normal. The heart was enlarged slightly to the left. The sounds were almost imperceptible. There were no murmurs or other abnormal observations. The pulse was 40 per minute, weak, and almost imperceptible. The blood pressure was 75 systolic and 40 diastolic. This was difficult to obtain accurately. Electrocardiograms were taken at this time and the patient was put to bed.

Urine, serologic and chemical blood examinations were negative. The treatment was not specific at this time because I did not know that the cause of the symptoms was aconitine poisoning. He was kept strictly in bed and given general stimulating treatment, including small doses of digitalis, thyroid extract,



Leads 1 and 2, showing increase in P-R interval.

½ grain (0.03 Gm.), three times a day, and potassium iodide, 10 grains (0.65 Gm.), three times a day. Atropine sulphate, 1/100 grain (0.6 mg.), by mouth was given two or three times but seemed to make the patient decidedly worse and had no apparent effect on the pulse. During the first week, he complained of occasional attacks of syncope even when he was lying in bed. His pulse became quite imperceptible at times, ranging from 40 to 48 per minute. His blood pressure remained about 80 systolic and from 40 to 50 diastolic. The second week his pulse became more rapid, his blood pressure rose, and he had fewer attacks of syncope. By the end of the fourth week, his blood pressure had reached 125 systolic and 80 diastolic, his pulse ran between 60 and 80. Throughout the entire illness the patient exhibited great anxiety and panic, and complained of uneasiness over the precordial area.

On examination of his activities preceding the onset of his illness it occurred to me to examine the whisky that he had imbibed the afternoon of his first attack. Analysis showed this to contain an alkaloid which on further examination proved to be aconitine. How this got into the whisky is not for me to decide. The whisky was bought at a more or less public source and for this reason it is possible that other similar cases are going about unrecognized. Examination of the electrocardiograms taken about eighteen hours after the ingestion of the poison revealed sinus bradycardia. Subsequent electrocardiograms revealed an increase in the P-R interval to 28. The most marked ones are reproduced herewith.

All accurate toxicologic knowledge is derived from experiments on animals. Here is a case of bradycardia and first degree heart block due undoubtedly to aconitine poisoning. No electrocardiogram on this patient is available before partaking of the offending beverage, but he had been in perfect health and outside of a left preponderance due to obesity there is no reason for suspecting a preexisting cardiac condition. He has now returned to normal health.

121 East Sixtieth Street.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, OCTOBER 25, 1930

THE COST OF MEDICAL CARE

The current situation so far as concerns solution of the problems of the cost of medical care is almost as cloudy and befogged as that of five years ago. The Committee on the Costs of Medical Care has supplied studies on which definite conclusions may be based. The numerous experiments in variations of the nature of medical practice existing in 1929 continue to exist, for the most part, although their conduct is constantly modified by new points of view, new details and the propaganda of the public press. The new experiments with clinics, hospitals, medical centers, institutes and what not are so recent that their effects are not yet measurable, nor is it possible to say whether or not similar organizations would function successfully in other communities.

The most recent publication of the Committee on the Costs of Medical Care concerns the contract medical service offered by the Endicott Johnson Company to its employees. That service is utilized by nine out of ten employees, wholly or in part. The investigation indicated apparently that a medical service so organized that there is no charge to the patient for each specific item permits wider use of medical facilities. This conclusion might be taken for granted. The study shows that in some respects contract service is the best type available but that in other respects it is below existing standards of practice. Actually, all that the Endicott Johnson Workers Medical Service demonstrates is the fact that it has been possible to establish such a service. The practitioners in the community not taking part in the contract service do as well financially as before, if not better.

In the current issue of the *Atlantic Monthly*, Mr. Evans Clark, an employee of the Twentieth Century Fund, founded by E. A. Filene of Boston, elucidates still further Mr. Filene's plan for medical guilds, which was brought out in THE JOURNAL some months ago. Mr. Clark argues for group practice, periodic examinations and health insurance. He wants specialized professional services at fixed annual fees, and he feels that it might be possible in this way with national organization to lower medical bills. Mr. Clark opposes the plan of charging more to the wealthy than is charged to the poor, notwithstanding the fact that he does not seem to have looked carefully into the basis for such charges. Actually, there is hardly a professional service available today, including that of ministers, lawyers, engineers, dentists and other professions, that does not charge on this basis. One cannot compare the importance of medical advice to a millionaire with the price of a box of strawberries. Apparently no one has raised the question as to why a lawyer will charge a millionaire more for making a will than he will a man with $100,000, when the man with $100,000 insists on distributing his money in such a fashion that the will requires twenty-five pages more than is required by the will of the millionaire who has decided to give all his money to his favorite friend. After all, the medical profession is becoming a little weary of suggestions for modification of its methods and customs by those who have never taken the trouble to find out those methods and customs, and the history of the reasons for their existence.

In the *Ladies' Home Journal*, Frederick L. Collins, professional writer, who has in the past discussed many subjects in many fields, now concerns himself with the high cost of being sick. His article is the kind of discussion that one might anticipate from a writer who had assembled a few references, looked at a few experiments, and attempted to draw conclusions covering the whole problem. Strangely enough, his illustrations are pictures of several of the wealthiest hospitals in New York City and do not concern the type of institution that has to administer to and care for the poor. His article is full, however, of sound but trite suggestions in this field.

Both Clark and Collins, as well as the editor of the *Ladies' Home Journal*, Loring A. Schuler, have come to the conclusion that lowering prices and state medicine are not the solution to the problem. Mr. Schuler concludes his editorial with the following significant statement:

> Much of the high cost of medical care is not due to the doctors, the system of treatment, excessive fees in nursing, hospitalization, or medical work. It is due to our own improper demands, to our expensive and usually ineffective attempts at self-medication.

In the meantime, attempts have been made to bring the most notorious experiment, the Public Health Institute of Chicago, under scientific auspices through the appointment of an investigating committee to analyze the qualities of its scientific work, and through the establishment of an advisory committee to consider ethical and social problems arising in the practice of the institution. Thus this experiment continues—tending apparently toward a form of practice that the medical profession can tolerate as safe, practical and scientific, and for the best interest of the science of medicine and the public.

The medical profession has lent itself willingly in the past and will, no doubt, lend itself willingly in the future to any experiment for solving medical economic problems that is established under good auspices, by leaders who are willing to play the game according to the rules. The rules are made primarily in the interest of the public. The individual who violates the rules in a zealous search for an answer to the problem may overstep the bounds and thereby suffer loss of his relationships to the organized medical profession. When he does so he is answerable for his own folly, since the organized medical profession has established means whereby any individual may assure himself that the system which he wishes to practice is for the public good and at the same time not a detriment to the practice of medicine. It is an aphorism that individuals pass from the scene but institutions of merit go on forever. The public must differentiate between the problem and the man. Occasionally a zealous officer of some component branch of organized medicine attempts, in his desire to uphold what he believes to be the rules of the profession, to employ extraordinary methods for the destruction of experiments. Appeals are made to public officials, the legal codes are scanned with a microscope, chambers of commerce are solicited for support and the signs of battle are kept constantly before the public. Individuals may voice personal opinions, not infrequently dictated by personal ambitions or political expediency or they may speak officially for medical organizations. The nature of the voice that speaks should always be made clear.

The great profession of medicine will go on, and the American Medical Association, established for the promotion of medical education, the advancement of medical science and the promotion of the public welfare, is not to be confused with any local issue until its official bodies have acted in relationship to such problems. The problem of providing the public with the best medical care at a price it can afford to pay has not been solved by the first three years of the five year experiment of the Committee on the Costs of Medical Care. It has not been solved by the establishment of sixty or more group clinics in the United States, by the notable success of one of these clinics or by the failure of many others. It has not been solved by the establishment of pay clinics in connection with hospitals, pay clinics established by universities, or commercial organizations organized by business men employing full-time physicians. It has not been solved by contract practice, by health insurance schemes, either compulsory or voluntary, or by the individual general practitioner. It is strange that physicians, who themselves distrust panaceas for diseases of the human body, should continually venture panaceas for the indispositions of the body politic. It is strange that public men who distrust one track systems in their commercial ventures should be willing to support similar systems for the solution of the problem of the cost of medical care.

THE ADVERTISING OF THE DENTIFRICE

The early part of the twentieth century may be interesting historically for the fact that it witnessed the apotheosis of the tooth brush, the tooth paste and the mouth wash. It started with the slogan "A Clean Tooth Never Decays," subsequently proved to be as false as many other slogans through which high pressure advertising agencies attract the shekels of the paying public. When the competition for maximum sales in tooth brushes was at its height, special claims were made for peculiar curves of the handle, unequal pieces of the tufting, hardness and softness of the bristles and a half dozen other alleged refinements that are less matters of scientific value than choice or taste.

So far as mouth washes are concerned, their virtues may lie in a slight astringency or alkalinity, in the mildly antiseptic influence they exert for the extremely brief period in which they are in contact with the oral tissues, or more probably in the fact that they contain enough water to provide a lavage appealing to the organoleptic senses. When Feasley thumbed the dictionary and found halitosis, he gave to Listerine a sales impulse that no other mouth wash has ever been able to equal. The conception embalmed in the title of a current refrain: "If Your Best Friend Won't Tell You, Why Should I?" has a psychologic urge that has caused hundreds of thousands of hoi polloi to burn the trails to the drug counter. Nor did the fact that the combination of substances included in Listerine is relatively ineffective and will not cure halitosis lessen the stampede. Furthermore, the promoters of mouth washes, like the promoters of every other article of merchandise from grapefruit to toilet paper, have secured testimonials from all sorts of people to the effect that they themselves have been benefited by actual trial of the substance concerned.

Recently, the Food and Drug Administration of the United States Department of Agriculture has cast a critical eye over the claims for antiseptic value made for various mouth washes and gargles. It is currently reported that the owners of all these bringers of gold are rushing hither and thither to the laboratories searching for substances that really are antiseptics and that can be added to their concoctions without changing taste or color—the important qualities—that the claims may be justified.

And now for the dentifrices! Through the potent spell of the comedy of Amos and Andy, a pepsinized mixture leaped to a leading position among tooth pastes, notwithstanding the lack of value of pepsin for this purpose. Claims made for alleged alkaline or acid values in tooth pastes have been strong—by contrast, as strong as the evidence to the effect that control of acid or alkali will prevent dental caries has been feeble. The changes have been rung long and insistently on alkalinity, on "the danger line" and on the percentage of those with pyorrhea. A half dozen assorted chemists

and the commissioner of health of New York assert that low surface tension means that a tooth paste will penetrate better between the teeth. The claim of special value because of low surface tension in connection with the selling of any tooth paste is one hundred per cent hokum. Any mixture of soap, glycerin and chalk, such as is available in many tooth pastes, would be equally endowed with a low surface tension.

The council on dental therapeutics of the American Dental Association has, it is reported, secured the promise of abandonment of the claims for low surface tension by the Colgate Company, and is actively endeavoring to bring other manufacturers of tooth pastes and dentifrices into the fold where claims made for products are substantiated by scientific evidence. Physicians should do all that they can to aid the American Dental Association in this campaign.

BRAIN FUNCTIONS

The problem of the localization of cerebral functions cannot be said as yet to have reached a definite solution. From the early days of scientific interest in the subject a century or more ago until the present time the pendulum of belief has swung from one extreme to another. Flourens convinced many of his contemporaries that the cerebrum is a single organ, functionally equivalent in all its parts. The subsequent work of experimentalists, notably Hitzig and Frisch and their followers, brought out "the overwhelming importance of the cortex." Before that period the corpus striatum was regarded as the great motor center, and the thalamus as the chief center of sensation. With the establishment of the highest cerebral centers in the brain cortex came extreme views of the localization of function in the brain in which the different motor and sensory areas were definitely circumscribed and separated from one another, making the cerebrum "a plurality of organs."

The more recent studies, as Howell [1] has pointed out, have tended to modify these extreme views of localization and to emphasize the fact that histologically and physiologically the entire cerebrum is connected so intimately, part to part, that, although the different regions mediate different functions, nevertheless an injury or defect in one part may influence to some extent the functionai value of all other regions in the organ. The general idea of a localization of function has been accepted, he adds, but the modern view is that the cerebrum is composed of a plurality of organs, not completely separated one from the other, as taught by Gall, but intimately associated and to a certain extent dependent one on another for their full functional importance.

It is not always easy to translate the results secured from animals in this field directly to human conditions. Accidents involving the brain and surgical necessities have therefore been depended on to supplement and substantiate the conclusions that have been developed regarding the functions of the human brain. Dandy [2] of the Johns Hopkins Hospital, from a series of cerebral operations of varying character, has reached the following conclusions:

> It is possible to remove all of the right cerebral hemisphere above the basal ganglia with no appreciable disturbance of mentality; this procedure has been carried out on several occasions for the removal of extensive tumors in the right hemisphere.
>
> On one occasion both frontal lobes have been completely extirpated for the treatment of a bilateral frontal brain tumor, and following this there has been no appreciable disturbance of mentality. The patient is perfectly oriented as to time, place and person; the memory is unimpaired; he reads, writes and conducts mathematical tests accurately; his conversation is seemingly perfectly normal.
>
> Furthermore, by the excision in other cases of the left occipital lobe and of the lower third of the left temporal lobe, we can be sure that none of these regions are responsible for intelligence. The intellect, therefore, is concerned with the remaining portion of the left cerebral hemisphere and is doubtless closely related to the speech mechanism.
>
> It has been found after ligation of the anterior cerebral artery on the left side that consciousness is completely and forever lost. This does not result when the same vessel is ligated on the right side. There is, therefore, within the limits of the distribution of this vessel an area specifically concerned with consciousness. The same result follows when this vessel is occluded at the middle of the corpus callosum, indicating that the seat of consciousness is posterior to this point in the vessel.
>
> The entire body of the corpus callosum may be split in the midline without any appreciable disturbance of function. This structure is, therefore, eliminated from participation in the important functions which hitherto have been ascribed to it.

When data of this sort become more abundant in the course of time, new synthetic conceptions and a better insight into the complicated nature of human cerebration will be realized.

Current Comment

ADVERTISING AND THE DOCTOR

The giving of a testimonial for a tooth paste by the commissioner of health of New York has been made the basis of an issue as to whether or not individual physicians and the medical profession should advertise. In a day when advertising and propaganda are the great gods of the American press, medical organizations have had to do their utmost to sustain the ethical principles that have guided the profession for many years. Those principles are not obsolete. They are as necessary for the maintenance of scientific medicine, for the good of the patient, and for the public health as is the golden rule. Organized medicine has championed willingly the abolishment of mystery from medical practice. It has given freely of its services for education of the public in hygiene and for information as to the progress that medicine has made in the control of preventable disease. A few county and state medical societies have

1. Howell, W. H.: A Text-Book of Physiology, ed. 10, Philadelphia, W. B. Saunders Company, 1927.

2. Dandy, W. E.: Changes in Our Conceptions of Localization of Certain Functions in the Brain, Am. J. Physiol. **93**: 643 (June) 1930.

used advertising space in promoting campaigns for the public health, in attacking quackery, and in education of the public. But as yet there is little, if any, proof that such campaigns have had results warranting the money spent on them. The secretary of one of the largest component societies of the American Medical Association has urged the employment of a public relations council for each medical group, and the employment of advertising space in the press for the promotion of medical interests, but he has been guided, no doubt, by the mere fact that great commercial organizations have promoted their interests in this manner. In a few instances physicians holding memberships in medical organizations have permitted the use of their names in the promotion of products in the health field, and in but few instances have the medical societies of which they were members called them to account. The testimonial given by the health commissioner of New York apparently aroused a storm of protest—not so much because it was a testimonial as for the fact that it represented a personal opinion not supported by adequate scientific evidence, and vaunting unduly the picture and personal qualities of the testimonial giver. The question in this case appears to be not so much one of medical ethics as of scientific judgment and good taste.

THE SEMICENTENNIAL OF A GREAT DISCOVERY

The week of November 2 will mark the fiftieth anniversary of the discovery, Nov. 6, 1880, of the parasites of malarial fever by Alphonse Laveran while an army surgeon in Algiers. Not long after, Sir Ronald Ross, then of the Indian Medical Service, proved experimentally that the malaria parasite is dependent on certain species of mosquitoes for its transmission from man to man. In 1897 he discovered the Laveran plasmodia in the stomach wall of *Anopheles* that had fed on the blood of malarial patients, subsequently proving that the spores of the parasites are concentrated in the salivary glands of the insect. In 1911 the American physicians Bass and Johns of New Orleans succeeded in developing pure cultures of the parasites of malaria outside the human body. These are some of the "high spots," passed in rapid review, of a series of scientific achievements in modern medicine that have been responsible for the prevention of much human suffering and the accomplishment of undertakings that were formerly regarded as well nigh impossible. Within the half century just passed, and during the lives of many still living, the old conceptions that malaria is caused by bad air, unwholesome odors, damp night winds, or impure drinking water have been dispelled forever, even from the minds of the untutored layman. Malaria has been eradicated from parts of the world. Without knowledge of its causative parasite and insect vectors, the Panama Canal could scarcely have been completed. A distinguished writer has remarked that the whole subject of malaria has become so fully clarified that a control of the scourge has become a matter for organization and administration alone. The golden jubilee of Laveran's pioneer contribution to the etiology of malaria coincides with the three hundredth anniversary of the earliest application of cinchona bark, with its quinine content, to the therapeutic management of the disease. As Bass [1] recently pointed out in THE JOURNAL, the cinchona alkaloids still constitute the only specific remedy for malaria. The methods for its prevention depend on the recognition of its cause, discovered by Laveran.

POLIOMYELITICIDAL ACTION OF NORMAL HUMAN SERUM

The serums of persons who have recovered from poliomyelitis usually, though not invariably, have the power of killing, neutralizing or inactivating poliomyelitis virus in vitro. It is generally assumed, though without actual experimental proof, that this neutralizing power is a measure of the probable therapeutic value of such serums. Relatively few control tests have been made with normal human serums, the general assumption being that, while such serums may occasionally neutralize poliomyelitis virus in vitro, they are usually inert or of such low viricidal power as to be of little or no therapeutic interest. A quite different perspective is suggested, however, by the report of Drs. Shaughnessy, Harmon and Gordon [2] of the Department of Hygiene of the University of Chicago. These investigators worked with Berkefeld filtrates of 5 per cent emulsions of spinal cords of infected monkeys. The filtrates were mixed with equal volumes of various dilutions of normal and convalescent human serum; the mixtures were incubated two hours and then stored in the ice chest over night. The next morning 2 cc. of each mixture was injected intracerebrally into a monkey, control injections being made with incubated mixtures of the same virus plus immune and nonimmune monkey serum. Of the twelve convalescent human serums thus far tested, eight neutralized their stock filtrate in a dilution of 1:2 and five in a dilution of 1:30. That is, only 40 per cent of their human convalescent serums were effective in vitro at this higher dilution, a dilution that corresponds to the maximum feasible therapeutic dose in human medicine. Nineteen serums from family contacts and normal children over 2 years of age were tested, seventeen of them neutralizing their virus in a dilution of 1:2 and fifteen, or nearly 80 per cent, in a dilution of 1:30. The investigators conclude from these data that serums of family contacts and of normal adults and older children possess greater power to neutralize poliomyelitis virus than the serums of persons who have recovered from an attack of the disease. They suggest that it would seem worth while in the light of these results for the clinician to study the value of selected normal serums, shown by laboratory test to neutralize virus, in the therapeusis of poliomyelitis. In this connection it may be recalled that more than a decade ago occasional favorable results with untested normal human serums were reported by Zingher.[3] Of even greater theoretical interest are the few tests made with serums of normal children under 2 years of age. Of the five

1. Bass, C. C.: The Treatment of Malaria, with Some Reference to Recently Promoted New Remedies, J. A. M. A. **95**: 988 (Oct. 4) 1930.
2. Shaughnessy, H. J.; Harmon, P. H., and Gordon, F. B.: Neutralization of the Virus of Poliomyelitis by Human Sera, Proc. Soc. Exper. Biol. & Med. **27**: 742 (May) 1930.
3. Zingher, Abraham: The Diagnosis and Serum Treatment of Anterior Poliomyelitis, J. A. M. A. **68**: 817 (March 17) 1917.

infantile serums thus far tested by the Chicago investigators, none neutralized poliomyelitis virus in a dilution as high as 1 : 10. Contrast this with the nearly 90 per cent neutralization at 1 : 10 dilution with the serums of normal children over 2 years of age. This observation seems to indicate that, in poliomyelitis, immunization of the normal infantile population proceeds in much the same way as is the case in diphtheria.

Association News

MEDICAL BROADCAST FOR THE WEEK

American Medical Association Health Talks

The American Medical Association broadcasts at 10 a. m. on Monday, 10:15 on Tuesday, and 10 on Saturday, over Station WBBM (770 kilocycles, or 389.4 meters).

The program for the week is as follows:

October 27. Not So Long Ago And Now.
October 28. What About Goiter?
November 1. Protecting the Mind of Childhood.

Five Minute Health Talks may be heard over the Columbia Broadcasting System daily except Sundays and holidays, from 12 to 12:05 p. m.

The program for the week is as follows:

October 27. Whither Goest Thou?
October 28. What Troubles Your Mind?
October 29. The Increasing Automobile Toll.
October 30. Worry Warps the World.
October 31. Be Sensible.
November 1. Sensible First Aid.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

CALIFORNIA

Personal.—Dr. Grafton Elliot Smith, professor of anatomy, University of London, England, will lecture at the University of California, November 18-19, on "Peking Men and Evolution of the Human Brain." Dr. Smith has held the position of professor of anatomy at the Universities of London and Manchester, and the Egyptian Government School of Medicine, Cairo, Egypt.

State Fair Exhibit.—The exhibit of the state department of public health in the educational building at the state fair held in Sacramento consisted of charts and models, illustrating the trend of births and deaths in the state. It was estimated that between 150,000 and 200,000 people visited the exhibit. Literature on public health subjects were distributed to all who expressed interest in the subject.

Society News.—The eighty-third semiannual meeting of the Southern California Medical Association will be held in the Hotel Virginia, Long Beach, October 31-November 1. The program includes "Deatness—A Vital Social, Economic and Medical Problem," Dr. F. L. Rogers, Long Beach; "The Dietary Factor in Kidney Disease," Dr. Noel F. Shambaugh, Long Beach; "Senility—Cause and Prevention," Dr. Paul B. Roen, Los Angeles; "Indications for Use of Special Tests by the Practitioner," Dr. Arthur L. Bloomfield, San Francisco; "Diagnosis and Treatment of Carcinoma of the Colon," Dr. James Tate Mason, Seattle; "Safety Margin in Nitrous Oxide-Oxygen Anesthesia," Dr. Harry K. Bonn, Los Angeles; "Nonoperative Treatment of Steer-Horn and Fish-Hook Type of Stomach," Dr. Harlan Shoemaker, Los Angeles; "Pyloric Stenosis," Drs. Burns S. Chaffee and Cleon C. Mason, Long Beach; "Chronic Meningococcic Septicemia," Dr. Fred B. Clarke, Long Beach; "Recent Developments in Our Knowledge of the Adrenals and Their Clinical Application," Dr. Burrell O. Raulston, Los Angeles; "Present Status of the Surgical Treatment of Benign Lesions of the Stomach and Duodenum," Dr. Verne C. Hunt, Los Angeles. Dr. Clay Ray Murray, New York, will present a talking motion picture entitled "Pott's Fracture," and Dr. Alfred C. Reed, San Francisco, an illustrated travelogue through Asia, "Tropical Diseases."——The San Francisco Pathologic Society was addressed, October 6, by Drs. Harold Brunn on "Echinococcus Cyst of the Liver"; Fred Firestone, "Hepatic Degeneration with Obstructive Type of Jaundice"; Stacy R. Mettier, "Hepatic Cirrhosis in a Young Woman"; Gordon E. Hein, "Macrophage Showers"; Alson R. Kilgore, "Unusual Goiters," and Edwin L. Bruck, "Epithelioma of the Stomach."——The Los Angeles County Medical Association was addressed, October 16, by Drs. Donald J. Frick on "The Heart in Diseases of the Thyroid Gland"; Oscar Reiss, "Report of 180 Cases of Poliomyelitis with Review of Present Epidemic," and Edward C. Moore and Donald G. Tollefson, "Hysterectomy."——The Los Angeles Trudeau Society will be addressed, October 28, by Drs. Edward W. Hayes, Monrovia, and John Dwight Davis on "The Practical Application of the Recent Classification of Tuberculosis in Children" and "Pathologic Changes of Lymph Nodes in Experimental Tuberculosis," respectively.

ILLINOIS

Society News.—The Taylorville Physicians' Club was addressed, September 24, by Dr. Perry E. Duncan, Chicago, on "Eye Injuries."——The Madison County Medical Society was addressed at Granite City, October 3, by Drs. Leslie D. Darner on gas poisoning, and Quitman U. Newell, St. Louis, cancer of the uterus.——At the annual meeting of the Tri-County Medical Society (Warren, Knox, Henry), October 13, at Galesburg, the speakers were Drs. Alexander A. Goldsmith, "Chronic Colitis"; Rollo K. Packard, "Surgical Mortality and Morbidity"; Edward L. Cornell gave an illustrated talk on obstetrics.

Chicago

Personal.—Dr. Le Roy Thompson was appointed chief of staff of the Illinois Charitable Eye and Ear Infirmary by Governor Emmerson, August 1, succeeding Dr. William L. Noble, and Dr. James L. Smith was appointed superintendent of the institution to succeed Dr. Leo Steiner.——Dr. Archibald V. Hill, Foulerton research professor of the Royal Society, London, England, lectured on "The State of Water in Tissues" at Northwestern University Medical School, October 20.

Society News.—The second William T. Belfield Lecture was given before a joint meeting of the Chicago Medical and Urological societies, October 22, by Dr. Edward L. Keyes, New York, on "Preventable Infections Incident to Preparing a Prostatic for Operation."——Dr. Joseph A. Capps delivered the presidential address before the Chicago Pathological Society, October 13, on "Pathogenesis of Cardiac Pain"; Dr. Harry Gideon Wells spoke on "Addison's Disease with Selective Destruction of the Suprarenal Cortex"; Dr. Phillip F. Shapiro, "Pathogenesis of Glomerulo- and Arterio-Necrosis in Malignant Nephrosclerosis," and William M. McGrath and Dr. Carl W. Apfelbach, "Spontaneous Bilateral Decapsulation of the Kidneys."——Dr. Ida C. Mann, London, England, addressed the Chicago Ophthalmological Society, October 13, on "Embryology of the Eye."——The Medical History Club of the College of Medicine of the University of Illinois opened its fourth season of public lectures, October 15. Dr. William F. Petersen spoke on "Count Struensee"; these lectures are held in the library of the college of medicine on the first and third Wednesdays of each month at 1 p. m.

INDIANA

Society News.—Dr. Bransford Lewis, St. Louis, addressed the Terre Haute Academy of Medicine, September 5, on "Movable Kidney."——The Floyd County Medical Society was addressed, October 10, at New Albany, by Dr. William F. Edwards on "Focal Infection."——Dr. Austin A. Hayden, Chicago, addressed the Indianapolis League for the Hard of Hearing, September 30, on "How the Handicap of Deafness May Be Overcome."

IOWA

Board of Health for University.—The board of health for the University of Iowa, authorized by President Walter Jessup, was recently organized and its divisional work inaugurated with headquarters at the student outpatient service offices. The personnel includes Dr. Henry S. Houghton, professor and dean of the college of medicine, chairman; Dr. Fred M. Smith, professor and head of the department of theory and practice of medicine; Dr. Milford E. Barnes, professor and head of the department of hygiene and preventive medicine,

secretary, and Carl E. Seashore, Ph.D., head of the department of psychology and the graduate college; Robert E. Rienow, dean of men; Miss Elizabeth Halsey, professor and head of the department of physical education for women, and Edward H. Lauer, Ph.D., professor and director of the division of physical education. With the approval of Dr. Daniel C. Steelsmith, state commissioner of health, the university board will enforce regulations of local health officers and remove possibilities of menace to health arising from the existence of the hitherto "no man's land" in the form of state owned properties. The activities of the new board will include the inspection division, under the direction of Jack J. Hinman, Jr., assistant professor of sanitation and chief of the water laboratory, which will carry out the sanitary inspection of all buildings under the direction of the quasi control of the university and all water, milk and food supplies and swimming pools. The communicable disease section, under Dr. Carl F. Jordan, assistant professor of hygiene and preventive medicine, will investigate and act on all reportable and communicable diseases within the university health district; those cases involving extramural action will have close cooperation with the local health authorities. The life extension division, under Dr. Chester I. Miller, chief of the student outpatient department, and Drs. L. B. Hanson and Grace E. Williams, examiners for men and women, respectively, will handle students, nurses and employees. The health examinations now required of all freshmen will be extended to include all incoming registrants and all prospective graduates during their final year. The student outpatient department will be supervised by Dr. Miller and will care for student illnesses, and those in need of additional service are referred to the hospital, for which a nominal charge is made.

KENTUCKY

Section Holds Annual Dinner.—The tenth annual session of the eye, ear, nose and throat section of the Kentucky State Medical Association was recently held in Louisville. Dr. Gaylord C. Hall, Louisville, presented his annual address on "Acute Retropharyngeal Abscess in Infants and Young Children." The guest of honor, Dr. John F. Barnhill, Indianapolis, spoke on "Headaches." The program included papers, among others, by Drs. Joseph A. Stucky, Lexington, on "Upper Respiratory Tract as a Guide to Nutritional Disaster—A Discussion of the Jarvis Syndrome"; Claude T. Wolfe, Louisville, "History and Diagnosis of Trachoma"; David L. Salmon, Madisonville, "Deformities of the Nasal Septum and Their Correction"; Harry D. Abell, Paducah, "A Questionnaire on Some of the Problems Concerning Tonsillectomy"; Will R. Pryor, Louisville, "Tuberculosis of the Larynx—Treatment with Actual Cautery"; Roy Glen Spurling, Louisville, "Diagnosis and Treatment of Brain Abscess," and Greenbury B. Brown, Jr., Lexington, "Causes of Bleeding from the Throat." Dr. William P. Drake, Bowling Green, was elected president.

MARYLAND

Another Cancer Clinic.—A cancer clinic was opened at the University of Maryland Hospital, Baltimore, October 6. It is located in the dispensary of the hospital at Lombard and Greene streets. The service will be free to all except those able to pay for diagnosis and treatment.

Dr. Doull Resigns.—Dr. James A. Doull recently resigned his position as coordinator of the study of common cold, which is being conducted at Johns Hopkins University School of Hygiene and Public Health, to become professor of hygiene and public health at Western Reserve University Medical School. Dr. Doull had been granted a leave of absence as professor of epidemiology at Johns Hopkins to carry on this work. The Chemical Foundation, a few years ago, gave $195,000 to the school of hygiene and public health for an exhaustive study of the origin, nature and possible cure of the common cold (THE JOURNAL, Jan. 21, 1928, p. 212; Aug. 4, 1928, p. 326). Dr. Vivian A. Van Volkenburgh, who has been a member of the staff of the school of hygiene and public health for several years, has been chosen to succeed Dr. Doull.

Society News.—The Baltimore City Medical Society held a symposium on duodenal ulcer, October 3. The society was addressed, October 17, among others, by Drs. Max Kahn on "The Question of Preoperative and Postoperative X-Ray Treatment of Cancer of the Breast," and Edward A. Looper, "Foreign Bodies in the Esophagus and Bronchi."——The semiannual meeting of the Medical and Chirurgical Faculty of Maryland was held in Westminster, October 22, at the Western Maryland College. Addresses were given by Drs. Frederick W. Wright on "The Entente—The Relationship of the General Practitioner and the Small Town Country Hospital to the Large Medical Center"; Charles C. Habliston and Thomas B. Aycock, "Phrenicotomy in the Treatment of Pulmonary Disease,"; Albert Austin Pearre, "Symptomatology of Hypothyroidism in the Adult," and William Francis Rienhoff, Jr., "Gastroduodenostomy."

MISSISSIPPI

Dr. Crider Goes to Jefferson Medical College.—Dr. Joseph O. Crider, dean and professor of physiology and histology at the University of Mississippi School of Medicine, University, resigned to become associate professor of physiology and assistant dean in the Jefferson Medical College, Philadelphia, where he assumed his new duties, September 22. Dr. Crider has been succeeded at the University of Mississippi by Dr. Philip L. Mull, professor of anatomy at the school.

NEBRASKA

Society News.—The Madison Five Counties Medical Society was addressed, August 26, by Drs. John J. Keegan on "Neuritis and Neuralgia," and Howard B. Hamilton, Omaha, "The Acute Abdomen in Young Children."——"Nephrosis" was the subject of Dr. Clark L. Phillips, Dixon, before the Cedar, Dakota, Dixon, Thurston and Wayne Counties Medical Society at Randolph, August 21. Dr. Paul F. Siman, Wayne, spoke on "Use of Foreign Protein in the Treatment of Peptic Ulcer"; Dr. Glen E. Peters, Randolph, "Undulant Fever" and Dr. Jacob N. Lande, Sioux City, "Some Diseases of the Skeleton in Infants and Children."——The Otoe County Medical Society was addressed at Nebraska City, September 8, by Drs. John Clyde Moore, Omaha, on "Serum Immunization in Children," and Abraham E. Bennett, Omaha, "Early Diagnosis and Treatment of Anterior Poliomyelitis"; Dr. Willis H. Taylor, Omaha, gave a screen lecture on some obstetric problems.——The Ninth Councilor District Medical Society was addressed at Grand Island, September 9, by Drs. Robert D. Schrock, Omaha, on "Fractures at the Elbow"; Eugene C. Foote, Hastings, "Eye Conditions in India"; Eli A. Watson, Grand Island, "Surgery of the Upper Abdomen," and Ernest Kelley, Omaha, "The Mechanism of Hysteria."

NEW JERSEY

Society News.—The Bergen County Medical Society was addressed, September 9, by Drs. Henry F. Helmholz, Rochester, Minn., on "Ketogenic Diet Treatment in Epilepsy"; John L. Morse, Boston, "Diagnosis and Prognosis in Pediatrics," and Russell Burton-Opitz, "Clinical Significance of High and Low Blood Pressure."——"Accessory Sinus Disease and Its Relation to Hay-Fever and Asthma" was the subject of Dr. Philip S. Stout, Philadelphia, before the September 10 meeting of the Burlington County Medical Society, and "Methods of Diagnosis of the More Common Diseases of the Ear," by Dr. Edward B. Gleason, Philadelphia.

Examination of Food Handlers.—The semiannual examination of all food handlers required by state board of health regulations, conducted by the Newark Department of Health, has been extended locally to include all domestic employees. Restaurant and kitchen employees must go to the department of health's clinic with the exception made for a few large department stores and insurance companies where complete clinical facilities are available. Ninety per cent of all other food handlers, including grocers, milk dealers, confectioners, bakers, butchers, soda dispensers and domestic employees, are examined at the clinics of the health department, but they have the option of examination by private physicians, who must use special blank forms. Examination for venereal diseases is made of all males. Routine swabs or cultures are not taken except when indications call for other specimens or a Wassermann test.

NEW YORK

Conference on Public Relations.—Thirty-one counties were represented at the first conference of the chairmen of public relations committees of county societies, held at Albany, September 18. Dr. James E. Sadlier, Poughkeepsie, chairman, outlined the work of the committee to consist of informing local physicians about services being conducted in the county, to establish a foundation for future health services by expanding work already undertaken, and to start new projects. The committee aims to establish cooperation between local physicians and volunteer health organizations and to promote a health survey of each county. The survey of Oswego is the fifteenth made under the auspices of this committee. Among its noteworthy results, especially in the cities of Fulton and Oswego, are the maintenance of a city welfare nurse to offer free services to families needing instruction in hygiene and care of the home and the child; the holding of prenatal clinics once a week, and the maintenance of a tuberculosis nurse for

the investigation of potential cases and free hospital provision for needy cases. The society cooperates with lay organizations in supplying free milk to poor undernourished children and in the campaign against diphtheria and smallpox. The child hygiene station and prenatal clinic training station for state welfare nurses was established and two specialists a month conducted clinics for children with mental deficiencies and for crippled children. Recommendations were made that efforts be directed to have all milk pasteurized and improvements made in the water supply and sewage disposal, and the establishment by the county of a dental clinic meeting alternately in Fulton and Oswego. The committee asked that physicians in localities where clinics are to be held should offer their services for a small consideration to be paid by the county in order to establish a permanent service to persons who cannot afford regular treatment.

New York City

Appropriations for Hospitals. — The board of estimate recently appropriated $600,000 for the immediate construction of buildings to house 800 additional tuberculosis patients, 503 of whom now await admission to city hospitals. The city hospital commissioner, Dr. J. G. William Greeff, in July had asked for $300,000 to build four fireproof pavilions at the farm colony on Staten Island for tuberculous patients, but when it was found that there was a great increase in the number of patients, provision for 800 additional beds were made without delay. The board also voted $300,000 for the reconstruction of the Brooklyn Cancer Institute. The commissioner stated that every institution for the treatment of tuberculosis is overcrowded with 10 per cent more patients than beds in the institutions. He reported that the number of city patients suffering from various diseases at its lowest ebb this year exceeded the highest number cared for last year. In the first six months of this year, 167,000 more visits were made to outpatient departments than in the whole of 1929. The daily census of the twenty-six institutions in the hospital department showed 1,500 more patients than were cared for last year.

Increase in Welfare Work.—The expenditures of relief funds by all social agencies of the city from 1910 to 1926 for health work increased from $136,000 to $466,000, and to help handicapped persons, from $10,000 to $278,000. The Welfare Council reports that the funds available to the thirty-eight principal organizations engaged in assisting persons in their own homes increased from $2,000,000 in 1910 to about $9,000,000 in 1926. The income of New York's privately supported relief agencies increased 300 per cent in seventeen years, and the income from municipal relief funds increased 2,500 per cent. Five per cent of the income comes from bequests and 76 per cent represents contributions from living persons and organizations. The trend of relief work is to enable individuals and families to solve problems that make them social work cases. Agencies have set up "sheltered workshops" where cripples, convalescents and other physically and mentally handicapped persons are enabled to support themselves fully or partially by work.

Society News.—Among the exhibits illustrative of phases of "Medical and Surgical Aspects of Acute Bacterial Infections" given at the third annual graduate fortnight at the New York Academy of Medicine, October 20-31, are those on undulant fever, Rocky Mountain spotted fever and tularemia through the courtesy of the National Institute of Public Health; dysentery, subacute bacterial endocarditis and colitis from the Army Medical Museum. Recent advances in bacteriology such as microbic dissociation and the Schwartzman phenomenon will be shown, and there will be a demonstration of bacteriophagy by Dr. Felix d'Herelle, New Haven, Conn.; postpartum infections from the Long Island College Hospital; subacute endocarditis, new type of bacterial toxins, and pathways of infections to the ear, from the Rockefeller Institute.——The twenty-fifth anniversary of the New York Society of Anesthetists, October 16-18, was addressed, among others, by Yandell Henderson, Ph.D., New Haven, Conn., on "The Anesthetist Therapeutist"; Dr. Irving L. Farr, Montclair, N. J., "The Psyche in Anesthesia"; Dr. Anna M. Stuart, Elmira, N. Y., "The Anesthetist Himself," and Dr. William Branower, New York, "General Anesthesia for Laryngectomy."

OHIO

Personal.—Dr. Harry L. Rockwood, commissioner of health of the city of Cleveland, has recently been announced as the new superintendent of the Mount Sinai Hospital. He will be succeeded by Dr. Harold J. Knapp. Dr. Rockwell has held the position of commissioner of health for twelve years.——Dr. Asher T. Childers, psychiatrist for Cuyahoga County Juvenile Court for the last two years, has been appointed chief of the psychiatric staff of Michigan.——Dr. Jackson Searles, Lisbon, has retired from medical practice to become a member of the faculty of the Ball State Teachers' College at Muncie, Ind. ——A complimentary dinner was given by colleagues to Dr. Valentino B. Di Loreto on his completion of twenty-five years in the practice of medicine in Steubenville.——Dr. Walter E. List, superintendent of the Minneapolis General Hospital, has been named superintendent of the Cincinnati Jewish Hospital.

Society News.—The Athens County Medical Society was addressed, October 6, by Dr. William Mithoefer, Cincinnati, on "Practical Points in Nasal Accessory Treatment."——The Toledo Academy of Medicine was addressed, October 3, by Dr. Jacob L. Bubis, Cleveland, on "Relation of Gynoplastic Repair to Modern Obstetrics."——A joint meeting of the Toledo Academy of Medicine and the Clinical Orthopedic Society will be addressed, October 31, by Dr. George W. Hawley, Bridgeport, Conn., on "Newer Apparatus in Treatment of Fractures of the Femur."——The Academy of Medicine of Cleveland was addressed, October 10, by Drs. Moses E. Blahd on "Spinal Anesthesia," and George Grey Turner, professor of surgery, University of Durham, and Hunterian professor and member of the council of the Royal College of Surgeons of England, Newcastle-on-Tyne, "Ruptured Gastric and Duodenal Ulcers." ——Dr. Franz Knoop delivered the twenty-third Hanna Lecture in the Institute of Pathology, Cleveland, on "The Significance of Intermediary Metabolism." Dr. Knoop is director of the Institute of Physiological Chemistry at the University of Tübingen, which professorship is said to be the oldest in Germany having been founded for Hoppe-Seyler.——Dr. Stuart Pritchard addressed the Eighth District Medical Society at Newark, October 2, on "Significance of the Cough as a Symptom." Dr. Pritchard made the trip from Battle Creek in his own monoplane.

OREGON

State Medical Election.—At the annual meeting of the Oregon State Medical Society, Portland, September 17-19, Dr. Thomas E. Griffith, The Dalles, was installed as president; Dr. Edward L. Zimmerman, Eugene, was made president-elect; Drs. Harvey J. Clements, Salem, John H. Fitzgibbon, Portland, and William T. Johnson, Corvallis, vice presidents; Drs. Richard H. Wellington and Frederick D. Stricker, Portland, treasurer and secretary, respectively, reelected. The next annual meeting will be held at Eugene. The revision of by-laws provided among other things the redistricting of the state into councilor districts. In the last four years, the society membership has increased more than 40 per cent.

PENNSYLVANIA

Fund for Institute of Mental Hygiene. — The Julius Rosenwald Fund has announced that a fund has been set aside to fill half of any deficit incurring up to a total of $17,500 for the first six years of the operation of the Mental Hygiene Institute of Pennsylvania Hospital. The purpose of the institute is to bring psychiatric service within the reach of persons of moderate means. In this country about 400,000 hospital beds are now used for mental patients.

Society News. — The Tenth Councilor District Medical Society and the Allegheny County Medical Society met jointly, October 21, and were addressed by Drs. John A. Heberling on "Diagnosis and Treatment of Early Joint Diseases"; George A. Holliday, "Arthritis in Infections of the Genito-Urinary System"; Paul B. Steele, "Acute Suppurative Arthritis," presentation of cases; Dewayne G. Richey, "Focal Infection in Rheumatic Fever, as Viewed by the Laryngologist," and Philip S. Hench, Rochester, Minn., "Clinical Consideration of Chronic Arthritis" and "Recent Progress in Study and Treatment of Rheumatic Diseases," illustrated.

Philadelphia

Personal.—Honorary degrees conferred at the celebration of medical progress at the University of Pennsylvania, October 10, included Surg. Gen. Hugh S. Cumming, Drs. James Ramsay Hunt, New York, William Gerry Morgan, Washington, D. C., Alfred Stengel, Alonzo Englebert Taylor, Stanford University, Calif., and William H. Welch, Baltimore, and Prof. Archibald V. Hill and Sir Walter M. Fletcher, London, England.

Prize in Pediatrics.—The Philadelphia Pediatric Society announces a prize competition to stimulate interest in pediatrics among practitioners of less than six years since graduation and residing in the Philadelphia metropolitan area. Investigations and studies to be presented must be limited to pediatric subjects. The first prize will be $100 and the second, $50, if the subjects submitted are of sufficient merit. Completed papers

must be in the hands of the chairman of the prize committee, Dr. Percival Nicholson, 16 West Montgomery Avenue, Ardmore, Pa., not later than November 15.

Research on Heart Disease.—The Robinette Foundation of the University of Pennsylvania has opened a new method of research in diseases of the heart. It was developed in connection with the study of the nature of the contraction of the heart muscles in which the electrocardiograph is synchronized with roentgen photography of the heart's movements. In this new field it is possible to time accurately any point on the curve of movement within one one-hundredth of a second of the corresponding event on the electrical curve of action. It has been found that certain types of diseases of the heart cause characteristic alterations from normal in curve of contact. In applying the technic of the study of the aorta, it is possible to obtain photographic records of human pulse waves and thus study the beginning of arteriosclerosis. The foundation, endowed by Edward Robinette, announced other projects at the celebration of medical progress at the University of Pennsylvania, October 10-11. Among these are studies of various social and economic groups, among which are 150 executives of a great corporation who carry the largest responsibilities, to determine the normal heart. The study of the familial relationships of heart disease has been instituted in heart clinics of the Pennsylvania Hospital with the support of the foundation. All available members of the family are given careful physical and mental examinations and subjected to laboratory tests to ascertain the influence of heredity on heart disease. The director of the Robinette Foundation is Dr. Charles C. Wolferth, assistant professor of medicine.

Society News.—The Philadelphia Academy of Surgery was addressed, October 6, by Drs. Irvin E. Deibert, Camden, N. J., and Francis C. Grant on "Observations on the Treatment of Osteomyelitis by the Orr Method" and "Results of Chorodotomy for the Relief of Pain," respectively.——The Pathological Society of Philadelphia was addressed, October 9, by Dr. Franz Knoop of the University of Tübingen on "Mutual Transformation of the Foodstuffs and Fixation of Nitrogen in the Body."——Drs. James S. Plant, Newark, N. J., and Max Levin addressed the Philadelphia Psychiatric Society, October 10, on "Importance of an Adequate Cause in the Prognosis of Praecox Types of Reaction" and "Archaic Mental Pneumonia as a Defense Reaction in Schizophrenia."——The October 8 meeting of the Philadelphia County Medical Society was given over to a symposium on the blood diseases; the speakers were Drs. Max M. Strumia, John Eiman, Harold W. Jones and William P. Belk.——The Philadelphia County Medical Society devoted its meeting, October 22, to a discussion of "Recent Applications of the Fundamental Sciences to Certain Medical Problems"; the speakers were Wilder D. Bancroft, Ph.D., "Some Recently Demonstrated Protein Reactions of the Nerve Tissues"; William Seifriz, Ph.D., "Medical Aspects of Certain Plant Reactions"; Dr. Stuart Mudd, "Studies of the Mechanism of Antibody Action"; Dr. Seymour Dewitt Ludlum, "Medical Principles in Neurological Diagnosis," and Dr. William Egbert Robertson, "Discussion of the Principles Presented and Their Relation to General Medicine."——Among others, Dr. William Jackson Merrill addressed the Philadelphia Pediatric Society, October 14, on "Appendicitis Simulating Acute Arthritis of Hip."——The West End Medical Society was addressed, October 15, by Drs. Joseph Bank and Samuel J. Goldberg on intestinal flatulence and bronchitis, respectively.

VIRGINIA

Continuation Courses for Practitioners.—The Norfolk County Medical Society's series of October meetings will mark the first anniversary of the continuation education course for practitioners conducted by the department of clinical education of the state medical society. The Norfolk County Medical Society was addressed, October 13, by Drs. Thomas V. Williamson on "Emergency Cystoscopy in Ureteral Calculus," and George W. Schenck, "Some Observations on Head Injuries." No attempt has been made to give comprehensive courses or fundamental basic science courses. These will be left to the regularly organized graduate courses of the medical colleges. The aim has been to teach the medicine of today to the general practitioner mainly by practical and nonoperative clinics and clinical conferences held in his own immediate vicinity. Addresses were given, October 20, by Drs. Walter B. Martin on "The Value of Iron in the Treatment of the Anemias"; October 23, Allie D. Morgan, "Treatment of Convergent Strabismus"; Levin F. Magruder, "Technic of Localization of Foreign Bodies in the Eye," illustrated; L. Leroy Jones, Portsmouth, "Treatment of Foreign Bodies Imbedded in the Cornea and Complications"; October 27, Dandridge P. West, "Three Years' Experience with Goat's Milk in Infant Feeding," and William L. Harris, "What Progress in Infant Feeding?" A course in practical psychiatry for students of the Medical College of Virginia will be given at the Central State Hospital at Petersburg. This is the second year that the state hospitals of Virginia have been opened publicly to the medical profession for clinical instruction. Members of the state society are requested to write for any information concerning the extension courses in graduate medical education to the chairman of the department of clinical education, 5 East Franklin Street, Richmond, or to Mr. George W. Eutsler, P. O. Box 707, University.

WISCONSIN

University News.—Student infirmary facilities at the University of Wisconsin will be virtually doubled by the recent action of the board of regents when it was decided to construct an addition to the present infirmary at a cost of $100,000. The student health and infirmary fee was increased to $4.50 a semester.

Personal.—Dr. William T. Pinkerton has resigned as medical director of the Prairie du Chien Sanatorium, a post which he has occupied, with one short interlude, for more than twenty-six years. Dr. Pinkerton, it is reported, will devote all his time to private practice.——Dr. John H. Connell, Beloit, has accepted a position as junior pathologist in the department of medicine of Tulane University of Louisiana, New Orleans.

State Medical Election.—At the annual meeting of the State Medical Society of Wisconsin, September 11, Dr. Cornelius A. Harper, Madison, was installed as president and Dr. Otho A. Fiedler, Sheboygan, made president-elect. The secretary will be elected by the council in January. The next annual session will be held at Madison in September. The society was the recipient of a gavel of historical interest presented by the Douglas County Medical Society. It was made from a portion of the keel of the boat *Algonquin* built in 1843, just two years after the establishment of the state society. The boat was the first vessel to sail Lake Superior. The gavel will be used in all future sessions of the house of delegates. The house adopted the recommendation to increase the dues of the society from $10 to $15 a year, to become effective in 1931. One third of all members of the society were in attendance at this session.

Society News.—The thirtieth annual meeting of the Tenth District Medical Society was addressed at Eau Claire, September 30, among others, by Drs. Louis E. Dougherty, St. Paul, and Francis D. Murphy, Milwaukee, on "Surgical Infections and Their Treatment" and "Diabetes: Its Complications and Its Management," respectively.——"A Differential Diagnosis of Ulcerative Conditions of the Face" was the subject of Dr. Edward Allen Oliver, Chicago, before the Medical Society of Milwaukee County, October 10, and "Significance of Pruritus in Medicine" that of Dr. Francis Eugene Senear, Chicago.——The Barron-Polk-Washburn-Sawyer-Burnett County Medical Society was addressed, September 5, by Dr. Arthur S. Hamilton, Minneapolis, on "Pain and Its Interpretation."——Dr. Chester M. Kurtz, Madison, spoke on "Diagnosis of Heart Disease from the Standpoint of the General Practitioner," and Dr. Phillips F. Greene, Madison, "Chinese Medicine" before the Trempealeau-Jackson-Buffalo County Medical Society, August 28.——The fall meeting of the Wisconsin Urological Society will be held at Madison, November 21; among the speakers will be Drs. Harry B. Culver, Chicago, whose subject will be "Management of Posterior Urethritis and Some of Its Complications"; Vincent J. O'Conor, Chicago, "Unilateral Hydronephrosis," and Hermon C. Bumpus, Jr., Rochester, Minn., "Uroselectan."

GENERAL

Institute for Radiological Research.—Announcement has been made of the recent formation of the Radiological Research Institute with Dr. Edwin C. Ernst, St. Louis, as president and Dr. Rollin H. Stevens, Detroit, secretary. This is a philanthropic organization whose object is to direct and coordinate research and to collect and disseminate knowledge in radiology gained as a result of purely scientific experiments or of experience in practical medicine which results have proved to be of the greatest value in medical practice, the arts and in industry. It aims also to render financial aid to research, to aid in the production of radium in this country with an effort to lower its cost, and to place newly developed apparatus where it will render the greatest service to humanity. The institute will fully cooperate with existing organizations interested in research pertaining to the study, diagnosis and treatment of diseases, especially cancer. In accordance with its provisions for fellowships in radiologic research, three fellowships have been established for research on roentgen apparatus.

Society News.—The next annual meeting of the Federation of American Societies for Experimental Biology will be held in Montreal, April 8-11, 1931; the secretary is Howard B. Lewis, Ph.D., University of Michigan Medical School, Ann Arbor. ——Dr. Frederick J. Taussig, St. Louis, was elected president of the Central Association of Obstetricians and Gynecologists at the annual session in Excelsior Springs, October 13, succeeding Dr. Palmer Findley, Omaha, the first president of the organization.——The annual meeting of the Western Surgical Association will be held at Kansas City, Mo., December 5-6, with headquarters at the Hotel Muehlebach; the secretary is Dr. Frank R. Teachenor, 306 East Twelfth Street, Kansas City.——At the annual meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons recently, Dr. Arthur H. Bill, Cleveland, was elected president, and Dr. Magnus A. Tate, Cincinnati, secretary. The next annual session will be held at White Sulphur Springs, W. Va., in September. —— The next annual meeting of the Society of American Bacteriologists will be held at Boston, December 29-31; the secretary is J. M. Sherman, Ph.D., Cornell University, Ithaca, N. Y.——The twenty-seventh annual meeting of the American Association of Railway Surgeons will be held in Chicago, November 5-7, with headquarters at the Hotel Sherman. The program will include a symposium on head injuries.

Sickness Among Wage Earners.—Dean K. Brundage of the U. S. Public Health Service, working for the division of research of the Milbank Memorial Fund, recently found that workers in industry are healthier than the general population of the United States. His investigations to ascertain the extent of the disabling sickness among wage earning adults were based on industrial morbidity data covering several years and showed that in manufacturing industries in the country as a whole about 80 per cent of the men are below the age of 45. A larger proportion of the female industrial workers, about 90 to 95 per cent, is below the age of 45. He found that between the ages of 15 and 20 the age curve of illness in a general population group mounts more rapidly than in a typical industrial group. In the general population the trend is steadily upward from the ages of 20 to 24, but among industrial employees the frequency rates rose slowly from the ages of 25 to 40 and then declined at the age of 60, followed by a resumption of the upward trend. During eight years between 1921 and 1928, inclusive, respiratory diseases caused one half of all disabling sicknesses; digestive disorders were second. Contagious and infectious diseases caused about 3 per cent of the cases. Women, especially those married, tended to be absent on account of illness from 50 to 100 per cent more often than men, especially for short periods. Excessive use of alcoholic stimulants was most pronounced among men doing the heaviest and most disagreeable work. An excess in the number of influenza victims was noted among miners and employees of dusty trades, and the incidence of pneumonia was marked among employees of metal industries.

The Poliomyelitis Situation. — Epidemic poliomyelitis shows an upward rise in incidence for the country as a whole. Five hundred and ninety-four cases were reported for the week ended September 27, which represents an increase of 100 over the preceding week, according to *Science News Letter*. Normally the seasonal increase would have reached its peak by the middle of October and additional reports should begin to show a decline in the number of cases. There are now more cases in the country than there have been for the last three years. The last large outbreak was in 1927 when at the peak 800 cases were reported and in the great epidemic of 1916 cases were reported by the thousands. In California, poliomyelitis showed a slight temporary rise after a recession in incidence. September 27, the disease was half as prevalent as in July. Increasing prevalence of the disease was noted in New York, Ohio, Kansas and other states, and in some communities drastic measures were inaugurated to curb the epidemic. Detroit has less than half the cases reported between January 1 and October 4, as compared with 1929, when there were seventy-eight cases. During September, officers of the Kansas Health Department made special efforts to check the rising incidence of poliomyelitis, especially in counties served by highways U. S. number 54 and U. S. number 81, where the disease seems to have centered. Newspaper reports showed an increase in prevalence of the disease during September in Minnesota, especially in twenty-three counties in the southwestern part of the state. Minnesota reported 205 cases and nine deaths over a six months' period. The state board of health has asked for an appropriation of $6,487.50 to aid in combating the disease. Ohio reported 100 cases recently. Other high figures were New York, 65; Illinois, 43; Massachusetts, 32; Maine, 21; Iowa, 21; Nebraska, 26; Wisconsin, 20, and Missouri, 18.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Oct. 4, 1930.

Early Treatment of Mental Disease

The board of control of the lunacy administration in its report points out that the event of the year was the passage of the mental treatment bill, which enables preventive treatment of incipient mental illness to be carried out by providing outpatient clinics for voluntary treatment, a great departure from the previous official practice, of certifying and confining in asylums persons who were sufficiently demented to be a nuisance or a danger. The treatment of mental illness is assimilated to that of other forms of illness by provisions under which certain cases may be temporarily placed under treatment in institutions without certification and by the opportunities afforded of associating the general hospitals in the treatment of mental illness. The board expresses the hope that local authorities will realize that, from the point of view of humanity and economy, treatment cannot begin too early, and will see that any charge made for the reception of voluntary patients shall not be such as to discourage admissions in the incipient stage. Attention is drawn to the important provision in the act for the temporary treatment of nonvolitional patients on the recommendation of two physicians without the intervention of any judicial authority. The object is to enable incipient mental cases to receive treatment without the stigma of certification. Treatment under this provision is limited to a maximum of six months, subject to permission from the board to extend it, if early recovery appears probable. Another change of great importance is the statutory recognition of the outpatient clinic. Local authorities are now empowered to provide such clinics or to arrange for their provision with the voluntary hospitals. The outpatient clinic is considered the most effective means of bringing within the reach of skilled treatment persons in the earliest stages of mental instability. When a clinic is established at a local hospital it is recommended that the medical staff of the local authority's mental hospital should be associated with the staff of the hospital in the work of the clinic. Local authorities are empowered to make provision for the after-care of patients who have undergone treatment and to contribute to the funds of voluntary associations formed for the purpose. An attempt is made in the act to remedy a great grievance of physicians who sign lunacy certificates—the worry and expense of having actions brought against them by litigious persons on regaining sufficient sanity to be discharged from an asylum. This danger is so great that many physicians decline to have anything to do with lunacy certification. The act provides that persons doing anything under it shall not be liable to legal proceedings if they have acted in good faith and with reasonable care, and the onus of proving the contrary will be on the plaintiff, who must obtain leave from a court to proceed with an action. This will not be given unless the court is satisfied that there is substantial ground for alleging that the defendant acted in bad faith or without reasonable care. A significant change in terminology has been made. It is provided that the term "mental hospital" may be substituted for "asylum" in all official documents. The number of persons of unsound mind under all forms of care increased during the year by 1,307, as compared with an average increase of 2,167 for the last five years. The total number of cases in England and Wales was 142,387, or nearly 3.6 per thousand of population.

Proposed Medical Socialist Organization

In THE JOURNAL, August 16, page 543, it was explained that the British Medical Association had brought forward a

scheme for a great extension of the form of medical socialism, known as national health insurance, not because either it or the medical profession desired this but because in the present socialistic phase of British politics they feared something worse —a state medical service. In both cases the state would provide a medical treatment for all, but, under the scheme of the association, physicians would continue to work under a contract and the profession would retain some autonomy. Under a state medical service they would simply be civil servants. In the medical profession there is a small body of socialists who desire such a service, and there is no doubt that the present socialist government would be pleased to introduce it if its hands were not so full of other problems. At the National Labor Club a meeting has been held to discuss the formation of a medical socialist organization. Dr. C. W. Brook, the convener, said that he had received a letter from Dr. Ewald Fabian of Berlin, stating that an international union of socialist physicians was about to be created. Dr. Brook advocated the formation of a medical socialist body on the following grounds: (1) as a means of pressing for the establishment of a properly organized national service, (2) as a means of contact through the International Union of Socialist Physicians with other national organizations, (3) as a means of devising legislation for the benefit of the health of the workers and of bringing pressure to bear on the authorities to carry it out, (4) as a means of propagating socialism in the medical profession (he would admit students as associates and so carry the campaign into the medical schools), and (5) as a means of working as an organized body of socialists within medicopolitical organizations. In the discussion that followed, Dr. Menon promised the support of Indian physicians in this country. The following resolution was passed unanimously: "That the members of the medical profession whose political views are in agreement with those of the labor party and with the ideals of socialism be organized as a political body and that a committee be formed to draw up a constitution."

Medical Tests for Automobile Drivers

Since the road traffic act was passed (THE JOURNAL, September 6, p. 738) the minister of transport and his officials have been busy with the necessary arrangements for bringing the various sections into operation. Many conferences have been held with automobile associations, manufacturers, insurance companies and trade unions representing members employed on road transport and bodies representing pedestrians. For the licensing of drivers there will be only one standard in all parts of the country. There will be two absolute bars to the granting of a driving license, even if the applicant already holds one. These are extremely defective eyesight and liability to disabling fits. Discussions are proceeding with the British Medical Association and with automobile organizations as to a scientific eyesight test. The broad principle to be adopted is the ability of the applicant to read the ordinary numbers of an automobile at a distance of 30 or 35 yards. Applicants will be required to state on their application forms that, so far as they know, they suffer from no complaint, such as heart attacks, epileptic fits or mental disease, which would interfere with their efficiency as drivers. If the applicant has any doubt he will be expected to take professional advice, as he will be liable to severe penalties for not disclosing essential facts. The disabled man presents some difficulty. If he already holds a license, it will be renewed if he declares that his driving has not been a source of danger to the public. A new applicant will be required to pass a driving test, of which details have been approved by representatives of automobile bodies and of the Disabled Men's Association. Applicants will also be required to produce a certificate that they are covered against third-party risks of death or bodily injury, and this certificate must be carried at all times.

PARIS

(From Our Regular Correspondent)

Oct. 1, 1930.

Neuritis in Drivers of Automobiles

During recent years, cervicobrachial neuritis has become a common manifestation in drivers of automobiles. It attacks almost exclusively those who drive closed cars and leave open constantly the window next to them; that is to say, it develops on the left side if the driver is seated to the left or on the right side if the steering wheel is located at the right. Left-drive cars are more numerous in France, since vehicles must keep to the right of the road, so that it is the left hand that is thrust out of the window in order to signal to the cars following that one intends to turn or to stop. The current of air that comes from the side, striking the shoulder and encircling the neck, causes, more especially on cold, damp days, the onset of the condition. The disorder is not found in drivers of open cars. It is a radicular neuritis of the brachial plexus, caused by an arthritis that has its seat at the level of the last cervical articulations, usually the fifth or the sixth. Pressure applied in that region will easily discover the painful spot. At this level, the periarticular swelling exerts a pressure on the medullary roots of the plexus. The pain has its seat in the shoulder and radiates toward the neck and the back. The circumflex nerve is most frequently affected, with the result that pains are provoked in the deltoid muscle and the brachial triceps. The pain is elicited by the movements that bring these muscles into action. But there are also spontaneous paroxysmal attacks lasting for several minutes, which come on in the evening, or at night especially, seriously disturbing sleep. The pains are exacerbated by cold and damp weather. This disorder attacks chiefly rheumatic subjects, and affects the elderly and aged more than it does young persons. Dr. Rathelot of Montpellier, who has published a monograph on this disease, refers to it quite aptly as "sciatica of the arm." The condition presents a similarity to sciatica. It is interesting to note also that, while in sciatica, in accordance with the Lasègue sign, an acute pain is elicited when the patient, while lying on his back, raises the leg, with the thigh flexed, toward the abdomen, a similar pain is provoked when the arm is extended horizontally and backward and the forearm is raised in supination, which brings about an elongation of the plexus. It is a condition that is not so easy to get rid of. Diathermy and infra-red rays have been employed without great success. Massage of the vertebrae is rather dangerous unless it is carried out with great prudence. The best treatment is exposure of the region to roentgen rays for ten minutes, twice a week, in small doses, for at least a month. Success has attended also local applications of radium, spread about in containers, for several days in succession.

Enlargement of the Radium Institute

Belgium radium continues to be sold at a high price, in spite of the competition offered by Russian radium; hence a large parcel of ground has been placed at the disposal of Madame Curie for the erection of a factory for the manufacture of radium. At the same time the Institut du radium, of which she is the codirector along with Professor Regaud, having outgrown its small quarters by reason of the afflux of patients, is to be enlarged, the city of Paris having placed at her disposal a large plot of ground contiguous to the institute, on which research laboratories and a hospital for the application of radium treatment will be built.

Trypanosomiasis in Kamerun

Severe criticism has been raised in Germany against the sanitary organization of Kamerun since, after the war, it ceased to be a protectorate of Germany and became a protectorate of France. It has been asserted that, while under German control, there were only 6,000 cases of trypanosomiasis in the country

and that now there are 315,000 cases. An article published by the colonial minister tones down these exaggerations. There are at present 115,000 cases. The Germans, however, had only two or three physicians prospecting in a fractional part of the country. There are at present eleven physicians, aided by native men nurses, with the result that they have explored the whole country and made an exact enumeration of cases. Isolation camps have been created where groups of patients are assembled and subjected to intensive treatment. It is thought that, within three years, the disease will have totally disappeared from the country, since the Belgians are carrying on the same intensive crusade in the neighboring Congo region.

Professor Censured for Advertising

The council of the syndicate of the physicians of the Seine (region of Paris) recently reached three decisions that it has made public through the press. The action of the council is without precedent and appears likely to create dissension in the medical profession. The syndicate is possibly within its rights in watching over the good name of the medical profession and in censuring confrères who have committed a tort against the rules of the profession; but heretofore it has never given public notice of the events. The first vote of censure expresses disapproval of the conduct of certain physicians occupying official positions at the Faculté de médecine and on the staffs of the hôpitaux de Paris, who, in public lectures and in the newspapers, took part in a controversy on the subject of the division of fees between the surgeon and the physician who refers patients to him. The resolution says: "These are matters that may be censurable or not, depending on the circumstances. The public is not to be the judge, and if misinformed, the public may get impressions that reflect on the credit of the whole profession." The second resolution censures physicians occupying an official position—professors, for example—who allow their names to be employed by a commercial house in order to promote the sales of a pharmaceutic specialty. It is evident that a certain professor is meant who, after publishing his articles on the use of magnesium chloride as a preventive of cancer and as a means of retarding the approach of old age, is said to have allowed his name to be used to promote the sales of a certain brand of magnesium chloride tablets. The third resolution is aimed against physicians who, in a recent edition of the official telephone directory, have had their names printed in display type, followed by statements as to the various diseases that they assert they are able to cure, in order to attract the attention of the public. For this privilege they pay, of course, an additional sum, so that it is, in reality, nothing other than a commercial advertisement. The council of the syndicate of physicians regards such procedures as reflections on the dignity of the profession and felt it was its duty to express its condemnation. It is the general opinion, however, that, while the censure may be justified, it would have been better if it had been expressed at a meeting of the council on medical ethics and not communicated to the public.

Houses of Prostitution Closed in Strasbourg

For many years there have existed in France houses termed "maisons de tolérance," occupied by prostitutes, who are subjected to periodic examinations. Two opposing groups of citizens have likewise existed for years, one of which argued for the regrettable but undoubted necessity of such places, in order to limit, by means of supervision, the propagation of venereal disease; the other group demanded that such places be suppressed in the name of morality and out of respect for the dignity of women, and for the reason that their effect on venereal prophylaxis is nil. In recent years an experiment has been tried in Strasbourg, where, in pursuance of a prefectural decree, such houses have been closed since Jan. 1, 1926. An endeavor has been made to discover whether, as a result of this closing measure, the cases of venereal disease in Strasbourg have increased or diminished. Statistics have been collected but their showings were interpreted so diversely that an official commission composed of Dr. Lévy-Bing, physician on the staff of the department for venereal women of the Infirmerie de la prison St. Lazare in Paris, Dr. Cavaillon, head of the prophylaxis service of the ministry of public health, and Madame Avril de Ste. Croix, president of the Conseil national des femmes françaises, was appointed to make an inquiry on the subject. The commission reached the following conclusions: The first two years that followed the closing of the "maisons de tolérance" in Strasbourg were followed by a marked increase of syphilis in that city. It is true, however, that these houses were nearly all transformed into saloons, or beer-shops, where prostitution, which had been open and supervised medically, became clandestine and unsupervised. During the next two years, however, there was a notable decrease in venereal disease, as confirmed by hospital reports and by the infirmaries at the garrisons. No exact statements can be made with reference to the cases cared for by the physicians in their private offices. The commission concluded that the closing of the "maisons de tolérance" has had no recognizable influence on the status of venereal disease in Strasbourg, and that the decline in the number of cases is more likely due to the greater intensity with which, of late, the antivenereal crusade has been waged.

MADRID

(From Our Regular Correspondent)

Sept. 25, 1930.

Self-Destruction in Twenty Years in Spain

Dr. Miguel España has prepared statistics on suicide in Spain in the period from 1907 to 1927. The rate in 1927 was 100 per million of population, which gives a total figure of 2,300 suicides for the year. During the twenty years, the number of suicides has been continually increasing. In 1907 the annual rate was 69 per million people and 1,050 men and 335 women did or attempted to commit suicide. In 1927 the suicides comprised 1,515 men and 528 women. The number of suicides committed during the twenty years was 31,261 (23,908 men and 7,353 women). The number of attempted suicides during the same period was 6,001 (3,632 men and 2,369 women). Among the men who killed themselves in 1907 there were 466 bachelors, 598 married men and 213 widowers. In 1927 the figures were 474 bachelors, 733 married men and 725 widowers. In the last year the number among married men and widowers was about the same. The month in which the fewest suicides occur is November; the month in which the largest number is committed is June. The method employed was as follows: firearms, 8,683 men and 509 women; swords and other cutting weapons, 2,110 men and 411 women; drowning, 3,904 men and 2,746 women; poisoning, 998 men and 2,177 women; hanging, 7,259 men and 2,012 women; asphyxia, 278 men and 116 women; leaping, 1,976 men and 1,282 women; by trains, 1,847 men and 347 women. The causes were: illness, 9,933 men and 4,000 women; disappointment, 2,122 men and 283 women; misfortune, 1,330 men and 94 women; misery, 871 men and 238 women; dismissal from positions, 171 men and 18 women; domestic troubles, 1,147 men and 832 women; love, 754 men and 703 women; jealousy, 128 men and 56 women; honor, 98 men and 119 women.

Intercontinental Transmission of Heart Sounds by Telephone

The Telephone Company of Spain gave recently a scientific demonstration to a group of physicians, consisting in the transmission of sounds of the heart and lungs of normal persons and patients with diseases of the heart and respiratory tract from Buenos Aires to Spain. The sounds were transmitted first by radio and then by telephone, so clearly that Spanish physicians who attended the demonstration were able to make a diagnosis in Spain at the same time that it was made at Buenos Aires

by Argentine physicians who were actually present with the patient. Then a discussion between Dr. Montellano, who was at Buenos Aires at the bedside of the patients, and the Argentine physicians followed the demonstration, and this was also transmitted by telephone. The diagnosis made by the Argentine physicians agreed with that made by the Spanish physicians. The demonstrations will be repeated, and physicians who wish to attend will be inscribed in a list, which at Madrid alone numbers more than 850.

Epilepsy

At the Academia Médico Quirúrgica of Madrid, Dr. Sanchiz Banus read a paper on epilepsy in which he said the disease is more common in men than in women, and that as a rule epileptic mothers transmit the disease to their male children while epileptic fathers transmit it to their female children. Headache in the patient or in near relatives has a relation to epilepsy. The speaker observed this symptom in 54 per cent of epileptic patients, in 64 per cent of mothers, in 8 per cent of fathers and in 24 per cent of near relatives of persons with epilepsy. The following familial characteristics were observed: an exaggerated feeling of mysticism in 24 per cent of the cases and pathologic irritability in 36 per cent of the cases. The speaker considered some accidents of a mechanical type during labor as a relatively frequent factor in the etiology of epilepsy.

Dr. Lopez Aydillo spoke on epileptic equivalents (headache, impulses, nocturnal enuresis, left-handedness, somnambulism, night terrors, dipsomania and narcolepsy) which he observed in 250 patients with typical epilepsy. Epileptic parents may transmit to their children either the disease itself or epileptic equivalents; parents who have epileptic equivalents may transmit either the epileptic equivalents which they have, or the disease itself which in them was not entirely developed, since both epilepsy and epileptic equivalents are originated from the same epileptic genotype.

Dr. Vallejo Nájera spoke on the medical treatment of epilepsy. Since the pathogenesis of the convulsions is unknown, the mechanism by which effective antiepileptic remedies control the crisis cannot be determined. Phenobarbital is the remedy that yields the best results against epilepsy, and next in importance is combined treatment with bromides and borates. A combined treatment of calcium and parathyroid extract reestablishes the calcium equilibrium of the blood. The results with the ketogenic diet are fair, but it offers difficulties which can be overcome only in infants.

Dr. Villaverde spoke on the surgical treatment of epilepsy. Lesions of the cornu ammonis, disappearance of myelin and atrophy of the brain convolutions have been observed in epilepsy. The speaker believes that the removal of the suprarenal glands and the resection of the superior cervical sympathetic ganglion of epileptic patients do not give satisfactory results. Trepanation, when used, should be made according to Kocher's method. Generally there is a pessimistic feeling against the few resources offered by surgery in the treatment of epilepsy.

False Diagnosis of Syphilis

At a meeting of the Academia Médico Quirúrgica of Madrid, Dr. Gay stated that in 7 per cent of the cases diagnosed as syphilis the diagnosis is wrong. The penal code of Spain imposes punishments for wrong diagnosis made on several conditions, but especially for the wrong diagnosis of syphilis. The speaker believes that the diagnosis of syphilis should be made on the basis of ultramicroscopic examinations of the lesions. Dr. Bejarano said that the average physician criticizes syphilologists because they seem to make a diagnosis of syphilis more frequently than the disease really is present. The speaker agrees that the diagnosis of syphilis should be based on ultramicroscopic observations of the lesions and not on the clinical symptoms presented by the patient. A weakly positive serologic reaction is not by itself an indication for antisyphilitic treatment. Dr. Covisa said that no antisyphilitic treatment should be given on the assumption of syphilis until the diagnosis of the disease is proved by the ultramicroscopic examination of the lesions, if the patient is in the first period of syphilis, or of a complete serologic examination if the patient is in the more advanced periods of the disease.

Serotherapy in Poliomyelitis

Dr. M. Bonavente recently presented a paper on poliomyelitis based on studies made at the Hospital del Niño Jesús during the last epidemic of poliomyelitis in Madrid. The author made the following conclusions: In the preparation of stock serums, careful asepsis is necessary. The activity of serums is in relation to their biochemical modifications. Serums reach their peak of activity in three or four months after their preparation. The author compared results obtained in poliomyelitis with the serum of convalescents and those obtained with serum of normal persons or antidiphtheritic serum and also with the cases in which no serotherapy was given. Patients treated with convalescent serum had a regression more rapid than those treated with other types of serum or those to whom no serum was given. Serum of convalescents should be given early in poliomyelitis to avoid spinal cord congestion and paralysis.

BERLIN

(From Our Regular Correspondent)

Sept. 29, 1930.

The Annual Meeting of German Scientists and Physicians

The Gesellschaft deutscher Naturforscher und Aerzte held its annual session in Königsberg, October 7-10. In his address of welcome, the Prussian *ministerpräsident*, Dr. Braun, said: "It is my heartfelt desire that your session may receive widespread attention in these days of political stress in our fatherland, far beyond the circles interested in pure science. It must be admitted that the quiet work of the scientific investigator is not yet appreciated in our country as it should be. The worship and glorification of the mailed fist observed today among our people constitute a sad and serious sign of mental aberration." It was pleasing to hear his enthusiastic words with reference to the heroism and the true leadership of the great scientific investigators who are working to promote the public health and to extend the bounds of knowledge, thereby setting goals for the oncoming generations to strive to reach and surpass.

The transactions gave an insight into many branches of scientific medicine; into the progress that is being made in all fields, and into the chief questions that, at present, occupy the minds of research workers and practitioners.

From the philosophic standpoint, the most important address was that of Prof. David Hilbert, mathematician, of Göttingen, who took as his subject "Naturkenntnis und Logik." According to Hilbert's conception of mathematics, it exerts an important influence on our view of the world and it may, in a sense, be said to constitute a world view in itself. The results of this exact science, which serves as an instrument of mediation between theory and practice and between thinking and observing, justify, he thinks, the declaration: "Instead of 'We cannot know,' our watchword must be: *we must know and we will know.*"

The second address was a memorial to Lothar Meyer. F. Paneth, chemist, of Königsberg, explained the development and the present status of our knowledge of the elements of the physical universe; the progress made in the study of the electrons, and the Rutherford-Bohr theory of electrically charged atoms. Since the research of Moseley, who fell in the battle of the Dardanelles, in 1915, not yet 28 years of age, we know that the positively charged nucleus constitutes the basis of the system of the elements and not, as Lothar Meyer and Mendelyeev had assumed, the atomic weight.

In the medical section, Hans Fischer, chemist, of Munich, who is also a physician, gave a comprehensive insight into the chemical connections between hemin, bilirubin and the porphyrins, adding many interesting physiologic and clinical observations. Some important connections with one of the greatest problems of organic chemistry were presented by the speaker and considerable light was thrown on them. These statements were supplemented by an address by Borst, pathologist, of Munich: "Morphologic Aspects of the Porphyrins." It became evident that his observations coincided closely with those of Fischer. Poppe of Rostock followed with a paper on "The Etiology, Pathogenesis and Experimental Diagnosis of Infection with Bacillus of Bang." W. Stepp, internist, of Breslau, gave an excellent clinical survey of this disease, which is at present in the forefront of medical interest. The most effective method of treatment consists in injections of increasing doses of killed Bang bacilli, which may now be procured in the open market.

The second general session was opened by Heinroth, zoologist, of Berlin, director of the Berlin Aquarium and the Rossitten ornithologic exhibit (Vogelwarte), who spoke on "Development of Early Bodily and Mental Characteristics in Domestic Birds."

Professor Bumke of Munich discussed with eloquence the topic of psychoanalysis. It is a natural corollary of the historical development of the theory of psychoanalysis, and also of its content, that the attitude of the individual investigator toward it must always be a subjective attitude. For almost thirty years, Bumke has been an opponent of this movement. While he recognizes the preeminent mental qualities of Freud, he rejects absolutely his teachings. But still more than the content of Freud's teachings, he opposes the methods on which Freud bases his teachings, because, in his opinion, they are not compatible with the principles of exact scientific research, since they cannot be checked up or substantiated by other investigators. After Bumke had described, in a few words, the attitude of various scientific investigators to Freud's theory, he mentioned the views of Thomas Mann, who has declared Freud's libido theory to be natural science in the form of romanticism and describes it as a manifestation of modern irrationalism. "Did Thomas Mann misunderstand Freud; do the rest of us who oppose him fail to comprehend him, or is (which appears more likely) psychoanalysis itself full of contradictions?" Charles Maylan, an adherent of psychoanalysis, thinks Freud has been misunderstood. According to Maylan, psychoanalysis was an outgrowth of Freud's resentment. His hatred of his father and of the pope, who is identified with the father and who, at the same time, is the head of christendom, and his dissatisfaction with scientific leaders, who withheld from him so long just recognition—all these feelings have tinged Freud's pen. One need not accept Maylan's interpretation, and one may even regret, for reasons affecting humanity in general, that the book was ever written. But one must admit that psychoanalysis did not come into being in the manner that its adherents maintain—by the application of an exact scientific method; by the establishment of incontroyertible facts and by a clear and intelligent study of such facts. Freud can perhaps be called, in one sense, a romanticist, because he does not derive his views from an application of his method but has had to adapt his method to fit his opinions. Freud's appearance on the horizon can best be understood by considering somewhat closely the period in which he began his work.

In the tenth decade of last century, there arose on the horizon two men, each appearing to possess the qualifications necessary for the creation of a new psychology: Dilthey and Freud. Dilthey was soon forgotten by the psychologists. Freud, with pronounced aptitude for psychology, has an artistic insight into the profound and obscure relationships of the psyche. He is fettered, however, by a materialistic attitude of mind. When he takes up scientific work, he has first to translate everything that is psychic into its biologic counterpart; he appears compelled to view his subject dynamically, from the standpoint of energy, and to talk about natural science when he really has in mind psychic relationships. When he comes in contact with the irrational or the subconscious, it has to be promptly rationalized and mechanized, and hypotheses are set up that may be regarded as irrational or, with equal correctness, as rudely materialistic. The subconscious with Freud is a subpsyche that elaborates the superconscious material supplied by the emotions and the intellect, but without furnishing the superconscious realm anything other than completed ideas. Bumke came to speak of Freud's interpretations—of the sexual substratum by and through which everything in the subconscious is regulated. He brought up interpretations of dreams as given by Freud, which are so schematized that one is reminded of translations made with the aid of a precise glossary. The real ego, which thinks and feels, desires, hates and loves, and which, above all, is "always sexually charged," not only deceives others but deludes and misleads constantly its own superconsciousness. The whole thing is assuredly a myth—not irrational, however, but puzzled out with all manner of subtlety and elaborated with all the devices of the dialectic art. A doctrine that constantly confuses possible with established facts, that does not distinguish between facts and interpretations, is not only not entitled to be classed under the natural sciences but is not entitled to be regarded as belonging to "science" at all. It lacks spontaneity because it comes from a cold and erratic intellect given over to gloomy speculation. A subconscious mind such as Freud describes—which thinks and feels—such a complicated subpsyche has never been shown to exist. There is, to be sure, a subconscious area, something that we do not wish to know and therefore thrust aside so far as possible. The double nature of the psyche has been recognized by poets. Faust has in Mephistopheles one who plays "opposite" to him; but Faust no longer needs Mephistopheles after his soul becomes purified. Were it not for this dualism of the soul there would be no particular merit, Bumke points out, for one to conduct himself fairly decently. As for the future of the freudian doctrine, Bumke ventures the opinion that the method will fall into desuetude because, in reality, it proves nothing and constantly distorts facts to fit its hypotheses. But certain perceptions, which are the products of the psychologic talent of their creator, will remain. The fundamental insight that the final goal of all psychology must be to comprehend man as a whole appears likely to be a permanent acquisition. Bumke's presentation was a rousing critical appeal, as Aschoff justly emphasized in his words of appreciation addressed to the author, and will cause every one to consider anew his attitude toward freudism.

The third speaker was Professor Teutschlaender of Heidelberg, who discussed "Cancer as a Disease Common to the Whole German People." About every tenth German who dies after the age of 40 dies from cancer. As in other countries, the mortality from cancer is increasing also in Germany, and it threatens to exceed that of tuberculosis. It is estimated that the annual number of cases in Germany ranges from 100,000 to 200,000 cases. The prevention of cancer is of the greatest importance. In the formation of cancer three factors of equal importance are involved: (1) an irritant acting on proliferative cells and set up by a factor acting from without or originating within the organism—the causative agent; (2) the predisposition, local or general disposition of the organism, which enables it to respond to the irritation set up by the causative agent with a cancer formation, and (3) in case the disposition is not yet fully developed, sufficient exposure; that is, the opportunity for sufficiently long action of the irritant. These three factors may vary as to their respective potencies, and particularly, one factor may be highly developed while the others are but weakly operative. Thus, cancer formation may sometimes be the

expression of an acquired or inherited constitution, or it may be conditioned by certain environmental factors or the subject's mode of living. The decisive specific factor does not attack from without; it lies or develops within the organism itself; it is endogenous. As there is virtually no contagion through cancer patients and also heredity plays no considerable rôle in man, the most important factor with reference to cancer disease as affecting the masses of the people is the nature of our present modern civilization, which, owing to the departures from nature in customs and habits of living and the ever increasing industrialization, brings about an enhancement of the three factors that play the chief part in the etiology of cancer. Evidence for the effects of our form of civilization on the spread of cancer is furnished, on the one hand, by the increased influence of a considerable number of etiologic factors, and, on the other hand, by the fact that today, to an ever increasing extent, cancers are diagnosed that owe their origin solely to the cultural trends and therefore may reasonably be termed "the cancers of modern civilization." The tar and dye industry, which dates its origin back less than a century, is putting daily on the market new products, some of which possess cancer-producing properties. The industry affords a wide field for the action of these products and, in fact, it arranges the tables for a veritable nation-wide experiment through industrial exposure, which, in turn, brings about a premature predisposition such as would not be acquired physiologically until a much later age is reached. The unsuitable diet of civilized nations may, on the one hand, through direct irritation of the mucosae of the digestive tract, and, secondly, by way of intoxications and disturbances of metabolism, exert a predisposing effect. In addition to the increasing number of occupational cancers, the cancers that develop from the habitual ingestion of arsenic may be regarded as cancers intimately associated with the nature of modern civilization. While it is doubtless true that many cancers are causally conditioned by our peculiar type of civilization, it would be wrong to consider all forms of cancer as the result of such influence. However, the increase in cancer is not a necessary accompaniment of civilized life as we know it, since we can already prevent occupational cancers and certain other cancerous formations not associated with our type of civilization. By destroying the evil effects of cancer-producing noxae—possibly also by bringing an influence to bear on constitutional factors—the spread of cancer must be combated, and already much has been accomplished in this direction by industrial hygiene. However, it will not be possible to eradicate cancer entirely with the sole application of hygienic measures. But with the aid of prophylactic measures, education, early treatment and the elimination of manifestations known as preconditions of cancer, which often cause patients little discomfort at the time, it must prove possible to reduce the number of cancer patients. It is better, and, as it seems, much easier, to prevent cancer than to cure it.

In addition, there were many special sessions on single subjects and combined subjects; thus, on radium surgery, roentgenologic diagnosis of the large intestine, benign disorders of the mammary gland and cancer of the breast, the rôle of the nucleus and the plasma in hereditary transmission, the migration of nematode larvae (with an excellent film), the origin of parasitic diseases in general, the eye and radiant energy, thrombosis and embolism, trachoma, social problems, and many other subjects of a similar nature. Professor Askanazy of Geneva explained the nature of the problem of comparative pathology, or a comparison of the pathologic phenomena of various peoples. The scope of the problem includes also the immunity or predisposition of the races with respect to individual diseases; the nature of the landscape as the source of a joyous disposition, of an earnest view of life and of resistance to disease. For general hygiene and for the prevention and cure of individual diseases, comparative pathology may have great value.

Marriages

ROBERT M. THOMAS, Oakland, Calif., to Miss Peggy Amelung of Los Angeles, in Worthington, Ohio, August 23.

JOHN WILLIAM HUFFMAN, Tucson, Ariz., to Miss Florence Kearnes of Evanston, Ill., August 18.

LAURENCE M. MOORE, Benton, Ill., to Miss Hazelle Dean Boland in Topeka, Kan., August 16.

GEORGE B. DORNBLASER, Hazelton, Pa., to Miss Grace Mildred Altmiller, August 12.

HOMER S. MCCOY, Sylvester, Ga., to Miss Eva Mae Bius, August 17.

Deaths

Hartstein Wendell Page, Worcester, Mass.; Medical School of Maine, Portland, 1888; member of the Massachusetts Medical Society, the American Psychiatric Association and the New England Society of Psychiatry; formerly superintendent of the Hospital Cottages for Children, Baldwinsville; aged 73; died, August 29, in York Beach, Me., of coronary thrombosis.

Thomas Benjamin Smiley ✠ Mount Vernon, S. D.; University of Bishop College Faculty of Medicine, Montreal, Que., Canada, 1893; past president of the South Dakota State Medical Association; delegate to the American Medical Association, 1911-1912; aged 64; died, September 29, of lymphatic leukemia.

Charles Bliss Stockwell, Port Huron, Mich.; Harvard University Medical School, Boston, 1878; member and past president of the Michigan State Medical Society; past president of St. Clair County Medical Society; aged 79; died, October 7, in Montour Falls, N. Y.

Charles E. Chapin ✠ Bloomington, Ill.; Rush Medical College, Chicago, 1891; past president of the McLean County Medical Society; medical director of the Brokaw Hospital; aged 64; died, September 26, of cerebral hemorrhage.

Adam Young Myers ✠ Hyndsville, N. Y.; Albany Medical College, 1882; past president of the Medical Society of Troy and Vicinity, and the Schoharie County Medical Society; aged 77; died, October 1, of cardiorenal disease.

Samuel Gayle Deatherage, Sugar Land, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1892; member of the State Medical Association of Texas; aged 59; died, June 5, in Missouri City, of myocarditis.

Samuel G. Worley, St. Augustine, Fla.; Atlanta Medical College, 1882; member of the Florida Medical Association; aged 74; died, in September, in a hospital at Grantville, Ga., of paralysis and hypostatic pneumonia.

John T. Perry ✠ Tulsa, Okla.; University of Arkansas School of Medicine, Little Rock, 1906; on the staff of the Morningside Hospital; aged 55; died, August 21, of septicemia following an infection on the face.

Norman William Andrews, Battle Creek, Mich.; University of Michigan Medical School, Ann Arbor, 1880; aged 72; died, September 13, in the University Hospital, Ann Arbor, of myocarditis.

McCord G. Roberts, Springfield, Mo.; St. Louis College of Physicians and Surgeons, 1891; member of the Missouri State Medical Association; aged 69; died, August 27, of cerebral hemorrhage.

George Clyde Ruble, Santa Ana, Calif.; University of Oklahoma School of Medicine, Oklahoma City, 1922; member of the California Medical Association; aged 31; died, June 3, of uremia.

Gilbert Haven Galford, Ashland, Wis.; Hahnemann Medical College and Hospital, Chicago, 1908; aged 47; was drowned, September 21, in the Chippewa River, when his boat was capsized.

Bennett Merwin Hines ✠ Uvalde, Texas; University of Nashville (Tenn.) Medical Department, 1894; city and county health officer; aged 60; died suddenly, August 28, of heart disease.

Clarence Eugene Bulette, Las Vegas, Nev.; Gross Medical College, 1897; aged 62; died, March 25, in the Ferguson Hospital, of chronic nephritis, myocarditis and arteriosclerosis.

Alfred Gideon Kyle, Knoxville, Tenn.; Memphis Hospital Medical College, 1900; member of the Tennessee State Medical Association; aged 66; died, August 30, of cardiorenal disease.

Bret Albert Swartz, Monrovia, Calif.; Medical Department of the University of Southern California, Los Angeles, 1917; aged 40; died, July 24, of pulmonary tuberculosis.

Matt Russell Root ✠ Denver; Colorado School of Medicine, Denver, 1897; member of the American College of Surgeons; aged 66; died, in September, of heart disease.

Claude A. Avery, Bethalto, Ill.; Barnes Medical College, St. Louis, 1903; member of the Illinois State Medical Society; aged 52; died, September 20, of heart disease.

Kurt L. Elsner, Brooklyn; Universitat Munchen Medizinische Fakultat, Munich, Bavaria, Germany, 1896; aged 57; died suddenly, September 17, of arteriosclerosis.

Frank Edgar Stowell ✠ Worcester, Mass.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1903; aged 51; died, August 31, of pulmonary tuberculosis.

Alexander Smith Sim ✠ Brooklyn; Long Island College Hospital, Brooklyn, 1904; served during the World War; aged 50; died, September 15, of heart disease.

Clareld Edison Dorland ✠ Devils Slide, Utah; Northwestern University School of Medicine, Chicago, 1907; aged 50; died, August 19, of cerebral hemorrhage.

William Kennedy Williams, Phoenixville, Pa.; State University of Iowa College of Medicine, Iowa City, 1880; aged 84; died, September 12, of uremia.

Glenn Raymond Ray, Decatur, Ill.; University of Illinois College of Medicine, Chicago, 1929; aged 27; was killed, September 15, in an automobile accident.

Walter Scott Spence ✠ Hopedale, Ohio; Medical Department of Western Reserve University, Cleveland, 1892; aged 64; died, September 19, of heart disease.

Henry Charles Towle ✠ Boston; Medical Department of the University of the City of New York, 1877; aged 78; died, September 5, of cerebral hemorrhage.

George O. W. Farnham, Lincoln, Neb.; University of Vermont College of Medicine, Burlington, 1884; died, September 5, of carcinoma of the stomach.

Mark Straus Polak, New York; Eclectic Medical College of the City of New York, 1892; aged 63; died, August 15, of carcinoma of the sigmoid flexure.

John William Shute, Bishop, Calif.; Hahnemann Hospital College of San Francisco, 1900; aged 62; died, July 23, of chronic parenchymatous nephritis.

John Anthon Callender, Oakland, Calif.; Medical Department of Columbia College, New York, 1868; aged 85; died, July 18, of cerebral hemorrhage.

Thomas Harrison Stetler, Pawpaw, Ill.; Chicago Medical College, 1876; aged 83; died, September 27, of uremic poisoning following chronic nephritis.

Griffith William Prees, Cambria, Wis.; Miami Medical College, Cincinnati, 1888; aged 79; died, September 8, of carcinoma of the stomach.

Charles H. Kaetel, Milwaukee; Pulte Medical College, Cincinnati, 1877; aged 80; died, September 6, of senile dementia and arteriosclerosis.

Noah Frederick Schmucker, Mount Jackson, Va.; Baltimore Medical College, 1897; aged 58; died, September 14, of diabetes mellitus.

Martin Luther Stiffler, St. Paul; University of Colorado School of Medicine, Denver, 1913; aged 43; died, September 7, of heart disease.

William J. Webb, Danville, Ill.; Columbus (Ohio) Medical College, 1884; aged 71; was found dead in bed, September 24, of heart disease.

John S. Cummins, Rosiclare, Ill.; Medical College of Evansville, Ind., 1883; aged 81; died, in September at Metropole, of arteriosclerosis.

Emmett B. McCormick, Owensboro, Ky.; Hospital College of Medicine, Louisville, 1881; aged 76; died, September 13, of heart disease.

Sefron C. Culpepper, Wiggins, Miss.; Louisville (Ky.) Medical College, 1894; aged 59; died, September 15, of pneumonia.

William S. Gordan, Converse, Ind.; American Medical College, St. Louis, 1890; aged 64; died, August 24, of heart disease.

Fred G. McMitchell, Gary, Ind.; Meharry Medical College, Nashville, Tenn., 1914; aged 50; died, July 30, of heart disease.

J. M. Blair, Monroe, N. C.; Louisville (Ky.) Medical College, 1887; aged 66; died, September 10, of cerebral hemorrhage.

Charles William Baker, Rossville, Tenn. (licensed, Tennessee, 1908); aged 58; died in August.

Bureau of Investigation

MORE MISBRANDED NOSTRUMS

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the United States Department of Agriculture

Michael's Cold Tablets.—The C. P. Products Company, Kokomo, Ind., shipped in December, 1928, into Illinois a quantity of Dr. Michael's Cold Tablets that were declared misbranded. They were found on analysis to be brown-coated tablets containing, essentially, acetanilide, sugar, talc, red pepper and a small amount of the laxative, phenolphthalein. The claims that it was a remedy for influenza, acute catarrh, neuralgia and fevers, and other conditions, were declared false and fraudulent. In April, 1929, judgment of condemnation and forfeiture was entered and the court ordered that the product be destroyed.—[*Notice of Judgment 16783; issued May, 1930.*]

Mosso's Oil of Salt.—The C. A. Mosso Laboratories of Chicago shipped in May, 1928, and January and April, 1929, a quantity of Mosso's Oil of Salt that was declared adulterated and misbranded. The federal chemists reported that the preparation consisted essentially of linseed oil, oil of turpentine, camphor and phenol, and that "bacteriological examination showed that the product was not antiseptic." The claims that the product would check infection, that it was antiseptic and germicidal, that it was a valuable aid in the treatment of pyorrhea and other diseases of the mouth and gums, that it would check the flow of blood, and that it would do many other things, were declared false and fraudulent. In June, 1929, judgment of condemnation and forfeiture was entered and the court ordered that the product be destroyed.—[*Notice of Judgment 16778; issued May, 1930.*]

OIL-of-SALT
The New Antiseptic and Healant
Keep a Supply Always on Hand in Home, Shop, Office or Factory
MOSSO'S
OIL of SALT
ANTISEPTIC
First Aid to the Injured
FIRST AID TO THE INJURED

[Mosso's Oil of Salt was analyzed in the A. M. A. Chemical Laboratory in 1915 and an article on the subject was prepared by the Bureau of Investigation and published in THE JOURNAL, August 14, 1915. The matter is reprinted in the pamphlet "Miscellaneous Nostrums."]

Nozeline.—The Nozeline Laboratory, Long Island City, N. Y., in January, 1929, shipped into New Jersey a quantity of Nozeline that was declared misbranded. Analysis by the federal chemists showed it to consist essentially of mineral oil, containing about 2 per cent of volatile matter, including eucalyptol, oil of pine, menthol and camphor. The claims on the trade package, to the effect that it was a remedy for catarrh, hay fever, throat ailments, nasal affections, etc., were declared false and fraudulent, and in July, 1929, judgment of condemnation and forfeiture was entered and the court ordered that the product be destroyed.—[*Notice of Judgment 16782; issued May, 1930.*]

Laxacold.—The Nyal Company, Detroit, Mich., in January, 1929, shipped into Illinois a quantity of Laxacold that was declared misbranded. The Laxacold tablets were found to contain acetanilide, alkaloids of aconite and of cinchona, extracts of plant drugs, including podophyllum and jalap, with camphor, red pepper, sulphates, and a small amount of salicylates. The

claims on the trade package, that the product would quickly relieve grippe, flu and neuralgia, were declared false and fraudulent, while the statement on the package, that the tablets were safe, was declared false and misleading. In April, 1929, judgment of condemnation and forfeiture was entered and the court ordered that the product be destroyed.—[*Notice of Judgment 16784; issued May, 1930.*]

Nyal Cold Capsules.—The Nyal Company of Detroit, Mich., shipped in September, 1928, into Illinois a quantity of Nyal Cold Capsules that were declared misbranded. The government chemists reported that the capsules contained acetanilide, chalk, cinchonine sulphate, and small amounts of red pepper, camphor, podophyllin, and the alkaloids of aconite. The claims on the trade package, that these capsules were a remedy for influenza, neuralgia, etc., were declared false and fraudulent, and the statement that the capsules were safe was declared false and misleading. In April, 1929, judgment of condemnation and forfeiture was entered and the court ordered that the product be destroyed.—[*Notice of Judgment 16785; issued May, 1930.*]

Diemer's Laxative Grip and Cold Tablets.—The Sta-Wel Remedy Company, Springfield, Mo., shipped in November, 1928, into Illinois a quantity of Dr. F. W. Diemer's Laxative Grip and Cold Tablets that were declared misbranded. The tablets were found to contain acetanilide, baking soda, red pepper and some laxative drugs. The claim that the tablets were a remedy for influenza was declared false and fraudulent and in April, 1929, judgment of condemnation and forfeiture was entered and the court ordered that the product be destroyed.—[*Notice of Judgment 16786; issued May, 1930.*]

Reno's Antiseptic Wash.—S. B. Leonardi and Company, New Rochelle, N. Y., shipped in May, 1928, to California a quantity of Reno's Antiseptic Wash that was declared adulterated and misbranded. The stuff was found to consist essentially of water (99 per cent) and small amounts of boric acid, camphor, and a trace of alkaloids. The federal authorities reported: "Bacteriological examination showed that the product was not antiseptic." The product was declared adulterated because it was sold as an antiseptic when it was not, and therefore fell below such professed standard. The claims that it was a remedy for leucorrhea, or "whites," and all discharges due to inflammation of the vaginal mucous membrane, were declared false and fraudulent. In August, 1929, judgment of condemnation and forfeiture was entered and the court ordered that the product be destroyed.—[*Notice of Judgment 16788; issued May, 1930.*]

Devel's Grippe.—The Devel's Chemical Company, Sylvester, Ga., shipped in January, 1929, into Florida a quantity of Devel's Grippe, which was declared misbranded. Analysis showed the product to consist essentially of extracts of plant drugs, including licorice and a laxative plant drug, with saccharine and volatile oils, including oil of anise, in a solution of alcohol and water. The claims that the product was a remedy for influenza, cough, fever, bronchitis, lumbago, neuralgia, and various other conditions, were declared false and fraudulent, and in September, 1929, judgment of condemnation and forfeiture was entered and the court ordered that the product be destroyed.—[*Notice of Judgment 16789; issued May, 1930.*]

Dionol.—The Dionol Company, Detroit, Mich., shipped into the District of Columbia in January, 1929, a quantity of Dionol that was declared misbranded. Government chemists reported that analysis showed the product to consist of white petrolatum! The curative claims for the preparation in such conditions as hemorrhoids, throat and lung diseases, infected wounds, pelvic congestion, etc., were declared false and fraudulent, and in August, 1929, judgment of condemnation and forfeiture was entered and the court ordered that the product be destroyed.—[*Notice of Judgment 16794; issued May, 1930.*]

[Dionol was the subject of brief reports in this department of THE JOURNAL, Jan. 26, 1918, and Feb. 7, 1920. The product was there declared to be a glorified and esoteric form of petrolatum.]

Correspondence

PRIORITY IN TREATMENT METHOD OF BROMIDE INTOXICATION

To the Editor:—In THE JOURNAL, July 12, Harris and Hauser published their paper on "Bromide Intoxication," in which success therapeutically depended on the replacement of bromine ions by chlorine ions; in this connection may I direct credit for originality where, I believe, credit is due.

The principle that the excretion of chlorides could be hastened by the administration of bromides and iodides, and that, conversely, the administration of chlorides hastens the elimination of the other two, was developed as far back as 1902 and 1911 (Sollmann: Manual of Pharmacology). Credit for the application of this biologic fact to therapeutics belongs, however, to the dermatologists Wile, Wright and Smith (*Arch. Dermat. & Syph.* **6**:529 [Nov.] 1922). A second report by Wile (*Arch. Dermat. & Syph.* **8**:407 [Sept.] 1923) in 1923 included the treatment of bromide intoxication as well as bromide dermatoses. Later, Stevenson (*Arch. Dermat. & Syph.* **12**:525 [Oct.] 1925) elaborated on the original work of Wile and his associates. Harris and Hauser failed to mention the work of Wile, Wright and Smith, and of Stevenson.

Furthermore, and apart from Harris and Hauser's report, the technic of Belote for the detection of bromides in the body fluids also deserves remention in connection with Wuth's paper (THE JOURNAL, June 25, 1927, p. 2013). It is a most simple test, involving the color change induced by bromine whereby the yellow of fluorescein paper becomes the pink of eosin (Belote: THE JOURNAL, May 28, 1927, p. 1696).

Without mention of these authors, the credit for an important and even life-saving method of treatment might be permanently lost.

FRED D. WEIDMAN, M.D., Philadelphia.

VIOSTEROL IN RICKETS

To the Editor:—I am much interested in your editorial comment in THE JOURNAL, September 13, on "Vitamin A in Disease." Toward the end of the editorial appears this statement: "Recently viosterol has come into vogue in the treatment and prevention of rickets. Because of its high vitamin D content it should be more valuable than cod liver oil, but in certain cases cod liver oil has seemed to be more curative than viosterol." Some research work that we have done at this institution with irradiated ergosterol as an antirachitic for chickens indicates clearly that the standard established for this product by the Council on Pharmacy and Chemistry of the American Medical Association is entirely out of line with the real antirachitic value of this product. We have fed irradiated ergosterol, or viosterol, in amounts theoretically equivalent to 2, 4, 6, 20, 50, 100 and 200 per cent of cod liver oil, and not until the last mentioned amount was included in the ration were we able to prevent rickets in chickens. As a matter of fact, even the lot receiving the theoretical equivalent of 200 per cent of cod liver oil in the form of viosterol was subnormal in bone ash and in bone structure as compared with the control lot which received 2 per cent of cod liver oil.

May I suggest that some of the early investigations with irradiated ergosterol may have resulted in faulty conclusions because rats were used as the experimental animals. Rats, of all animals available for rickets work, appear to be least desirable because the species has been evoluting in dark and shadowy environments for a million years or more, and consequently the type with the lowest ultraviolet or D requirement has been evolved. The fact that thousands of rats were used in various vitamin research experiments before the D factor was discov-

ered indicates that rats have an extremely low requirement for this factor. Birds, on the other hand, have a relatively high D requirement because of their evolutionary background. We do not suggest that birds are exactly the ideal type for D research work, but do feel that faulty conclusions are being reached through the use of rats for this particular type of experimentation.

So far as we can determine from a review of the literature, there are no data from experiments with human beings that would conclusively indicate that the Council on Pharmacy and Chemistry standards for viosterol are correct.

F. E. MUSSEHL, Lincoln, Neb.
Chairman, Poultry Husbandry Department,
College of Agriculture.

Queries and Minor Notes

ANONYMOUS COMMUNICATIONS and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted on request.

MEDICAL AND ETHICAL ASPECTS OF STERILIZATION

To the Editor:—I am engaged in medical missionary work in a thickly inhabited district of China. Part of my time is spent at a foundling asylum. As is well known, China is overpopulated and the birth rate is high. There is little knowledge of birth control, and abortion is comparatively uncommon. Two factors that offset to some extent this situation are high infant mortality and the refusal on the part of many families to rear their babies. The first is intolerable from a medical standpoint. The second is intolerable from a moral point of view. My questions, then, are: 1. Has modern gynecology any fairly reliable surgical procedure for sterilizing women which is practicable by an ordinarily trained surgeon? 2. Does such a procedure have any deleterious effect on the personality and sex life of a woman? 3. What, in your opinion, would be the attitude of reasonable and ethical medical men toward such a proposition as this: That any woman who has four living children may apply to a hospital and have the sterilizing procedure carried out if her health permits, with no embarrassing insinuations made, and at a minimum of expense—possibly paid by the state?

GEORGE THORNGATE, M.D., Liuho, Kiangsu, China.

ANSWER.—1. There are a number of fairly reliable surgical procedures for sterilizing women, but not one of them is absolutely dependable except removal of all ovarian tissue. The roentgen rays and radium may also be used to produce sterility, but they have the disadvantage of bringing about an artificial menopause. The simplest surgical treatment is that recommended by R. L. Dickinson; namely, occlusion of the tubal openings inside the uterine cavity by means of an electric cautery. This method, however, is not much used. Among the intra-abdominal procedures the one most commonly employed is the following: A ligature is placed around the tube about 2 cm. from the uterine cornu. The uterocornual junction is excised, the proximal end of the tube is buried within the folds of the broad ligament, and the cornu of the uterus is sutured and covered with peritoneum. The same procedure is carried out on the opposite side. A much simpler and just as effective method is the Madlener operation, which consists of elevating the midportion of each tube, gently but firmly crushing it with a smooth clamp, and placing a heavy silk ligature in the groove produced by the clamp. This method is simple, bloodless and quickly performed and is especially useful when sterilization is necessary at the time a cesarean section or hysterotomy is performed.

2. Sterilization operations performed on the tubes have no effect on the personality or sex life of the individual. If the patient is not informed of what has been done, she will have no subjective or objective indications that she has been sterilized other than that she cannot conceive.

3. This question is a complex one and should be answered by sociologists, not by medical men. On purely medical grounds there is no reason to refuse such a request, although at the present time the usual indication for sterilization is just the reverse of the one mentioned. Practically the only time sterilization is now carried out is for some serious medical ailment. An exception to this is the woman who has had a number of cesarean sections. Undoubtedly if such a proposition were made to medical men, many of them would oppose it because of religious beliefs.

OBESITY AND GLYCOSURIA

To the Editor:—A man, aged 54, obese, weighing about 280 pounds (127 Kg.), and about 5 feet 6½ inches (167.7 cm.) tall, has had a constant glycosuria for the past three years. Previous to this, it was an intermittent one. His blood sugar was 210 mg. per hundred cubic centimeters of blood about three years ago. Several weeks ago his blood sugar was 360 mg. A quantitative examination of the sugar in the urine showed about 5.5 per cent sugar. No acetone or diacetic acid was found in the urine. The patient's weight is constant and has not diminished for the past seven years. He has symptoms that point to a nerve involvement and has numbness of the feet, especially the heels. He also complains of indefinite pain in the epigastrium. Will you kindly state whether insulin is indicated and how much in this case because of the high percentage of sugar in the urine and the high sugar content of the blood? The patient has been on a diet all this while which, however, is not sufficient to control the glycosuria. What is the likely cause of this pain in the abdomen? It has no relationship to meals, coming on at irregular times. The patient is a clerical man. Kindly omit name.

M.D., Wisconsin.

ANSWER.—Analysis of this story makes it seem highly probable that unless a diet is instituted which will result in the patient losing considerable weight there is little chance of reducing either his glycosuria or his hyperglycemia. The experience with patients of this type suggests, as Joslin has so frequently pointed out, is that the obesity is a precursor to the diabetes; and a man of these dimensions is certainly tremendously overweight. It is also true that many patients of this type who claim to be on a diet actually are not, for the diet in such a patient must be low in calories as well as in carbohydrate.

The description of the various pains suggests diabetic neuritis. It does not seem wise to use insulin at the present time for a simple reason: Insulin will result in the utilization of more food, and therefore an increase in weight. A vicious circle is thus established. Perhaps under careful dietary control the patient will become sugar free but, if not, it might be wise to reduce his fat intake tremendously and give him small doses of insulin to assist in the utilization of what carbohydrates are necessary. This type of diet has been described by Evans and Strang.

DIET RESTRICTIONS WITH MILD MERCUROUS CHLORIDE (CALOMEL)

To the Editor:—Please express the present-day thought as to dietary restrictions applying to a patient taking calomel, with particular reference to fruit and vegetable acids, and to milk. Kindly omit name.

M.D., West Virginia.

ANSWER.—There is no scientific reason for dietary restriction or avoidance of acid fruits in connection with the use of mild mercurous chloride.

EFFECTS OF SODIUM NITRATE IN POWDER MANUFACTURE

To the Editor:—We (Apache Powder Company) are interested in the literature on the subject of the untoward effects of prolonged exposure to sodium nitrate in the manufacture of powder. We have an employee who has worked in the nitrate for the most of his eleven years' employment and who has low blood pressure, low hemoglobin and low basal metabolism alleged to be due to exposure to sodium nitrate. However, he has also Argyll Robertson pupils, diminished knee jerks, ataxic gait and positive Romberg sign, which suggests tabes; but the blood and spinal fluid Wassermann, Kahn and serum globulin reactions and the colloidal gold curve are all negative. Therefore we are interested to know what, if anything, has been written on the effect of exposure to sodium nitrate on man, and will appreciate any information you may supply as to where we can find reference to such literature.

R. C. KIRKWOOD, M.D., Benson, Ariz.

ANSWER.—For generations nitrates have been manipulated by workers, in the manufacture of explosives, without having attracted the attention of industrial hygienists or toxicologists as a source of harm. The inference is that these substances are not frequent causes of significant harm to workmen. Opinions as to sodium nitrate toxicity are largely based on its chemical similarity to potassium nitrate, more being known about the toxic properties of the latter. Acute poisonings from accidental ingestion of nitrates are well known. This phase is well covered by Peterson, Haines and Webster in their textbook "Legal Medicine and Toxicology" (Philadelphia, W. B. Saunders Company, 1923). A fatal case of nitrate poisoning was described in THE JOURNAL by Windmueller (Sept. 10, 1921, p. 858). Additional data may be derived from Sollmann's "Manual of Pharmacology" (Philadelphia, W. B. Saunders Company, 1927) and Solis-Cohen's "Pharmaco-Therapeutics" (New York, D. Appleton & Co., 1928).

From all sources it seems likely that nitrates are changed to nitrites to some extent in the body, and that bodily responses are in part characteristic of the latter. Lowered blood pressures, anemia and subnormal metabolic rates have been described. Diuresis, gastro-enteritis, myalgias, partial blindness and tachycardia likewise have been observed. Windmueller's patient presented manifestations quite dissimilar to those indicated in this query.

AUFRECHT'S METHOD OF TREATING PNEUMONIA

To the Editor:—May I have details of Aufrecht's method of the treatment of pneumonia by means of injections of quinine?

J. C. PARHAM, M.D., Port au Prince, Haiti.

ANSWER.—Aufrecht said in a recent article that the prescription he uses consists of 2 Gm. of quinine hydrochloride, 1 Gm. of urethane (ethyl carbamide), and 20 Gm. of distilled water. The urethane permits the dissolving of the quinine hydrochloride in a small quantity of water. When this mixture is used, 0.5 Gm. of quinine hydrochloride can be administered in 5 Gm. of fluid. The usual number of injections required is two or three, given at twelve or twenty-four hour intervals. The best site for the injections, Aufrecht said, are the lateral abdominal walls. If the injection is made carefully and the needle removed slowly by pressing a cotton compress on the skin around the puncture, there is no bleeding and the injected fluid spreads easily in the loose tissue. When the distilled water is too cold, the quinine precipitates, but it can be dissolved again if the container is placed in a warm water bath. Aufrecht employed quinine therapy only in lobar pneumonia and not in bronchopneumonia or pneumonia due to the Friedländer bacillus. All his patients were adults. In several hundred cases treated he did not note any complications. Aufrecht injected the quinine subcutaneously. Berger reports favorable results with injections intramuscularly into the extensor muscles of the thigh. Although quinine has been used in the treatment of pneumonia, its value has not yet been fully demonstrated; furthermore, all recent work seems to show that intramuscular injections are absorbed less efficiently than oral.

THE ANOPHELES AND MALARIA

To the Editor:—In the past, malarial infection was said to be carried by the anopheles mosquito. Recently in Lake County, Ind., there have been reported various cases of malaria. Is there any recent report that malaria may be transmitted by other mosquitoes besides anopheles?

B. B. REEVE, M.D., Whiting, Ind.

ANSWER.—It is accepted as almost a truism that human malaria can be transmitted only by anophelene mosquitoes. Certainly there is an enormous literature proving the importance of anophelenes and there are no recent reports giving any valid evidence that mosquitoes, other than anophelenes, can carry the disease. The fact that anophelenes are so important has served to lessen interest in the culicine species and as a consequence there is little carefully controlled experimental work showing that the culicine species cannot be infected with human malaria.

The recent work of C. G. Huff on avian malaria (which is generally carried by culicine species) is interesting in this connection (*Ann. Trop Med.* **23**:427 [Dec.] 1929). He finds that the susceptibility of mosquitoes to malaria is not solely a species characteristic but is largely an individual idiosyncrasy determined by heredity. This probably will help to explain why a given species of anopheles may be a dangerous carrier in one locality and not in another. Huff also believes that it is likely that if a large number of culicines were fed on infected human beings a few would become infected. All of this is highly speculative and must await further experimental work.

ANNULUS OF VIEUSSENS

To the Editor:—What is the "annulus of Vieussens" that Sutton and Lueth removed so often? My dictionary defines it as the same as "annulus ovalis," which is the "margin of the septum of the foramen ovale of the fetal heart." I don't see how they could have gotten away with the resection of that or how it would have given the results they obtained from its extirpation.

L. M. BLACKFORD, M.D., Atlanta.

ANSWER.—The ansa subclava of Vieussens is the more anterior of two sympathetic nerve bundles connecting the middle and inferior cervical ganglions of the sympathetic on each side of the neck. This nerve bundle, instead of going directly from the middle to the inferior ganglion, extends downward in front of the subclavian artery, and turns backward beneath that artery and then upward behind it to join the inferior ganglion. On its course it usually gives off a middle cardiac nerve and a filament to the recurrent nerve as it extends upward from the vagus to the esophagus, trachea and larynx. The reason for the curious course of this bundle is that during development the subclavian artery on each side has moved caudad from its primary position in the front of the neck, descending in front of the inferior ganglion and thus producing an elongation of that bundle of nerve fibers connecting the two ganglions in front of it while the other bundle connecting the two ganglions behind it remains of the same length. This ansa, described by the French anatomist Vieussens about 1700 A. D., must not be confused with the ring of musculofibrous tissue (annulus ovalis Vieussenni) which surrounds the foramen ovale and the septum ovale of the heart, which he also described.

TREATMENT OF PARKINSONIAN DISEASE WITH STRAMONIUM

To the Editor:—I have been afflicted with parkinsonian disease for five years. I have taken scopolamine, 1/150 grain (0.4 mg.), three times a day; parathyroid, 1/10 grain (6 mg.) daily, also autocondensation, which seems to help a little. Can you suggest anything in the way of treatment; e. g., stramonium? My worst symptom is the tremor.

M.D., Oregon.

ANSWER.—Stramonium, perhaps more than scopolamine, does seem to have some effect in reducing the rigidity of the parkinsonian syndrome that follows epidemic encephalitis, though they have little effect on the tremor, as a rule, and are of little value in true Parkinson's disease or paralysis agitans. Nothing that has yet been discovered has much influence in most cases in this last condition.

SENSITIVITY TO HEAT AND COLD

To the Editor:—I have a case which is giving me, as well as others, a real workout: A man, aged 55, of rather spare build, well nourished, had gallbladder drainage several years ago. About three years ago he developed a skin condition which gives him real annoyance. It itches continually and on being scratched leaves small scabs. The patient can remain indoors for two weeks and it completely disappears, but when he goes out again in sun, wind and dust, it immediately reappears. He has been through several clinics without result. He has just come home from the University Hospital at Omaha after a stay of several weeks, during which no infection or organic trouble was found. The skin department diagnosed the trouble as eczema of the neurodermic type and put him on sodium thiosulphate, 1 Gm. intravenously every two weeks, and I am still giving this treatment. He has tried other treatment without results. If you can give me any pointers it will be greatly appreciated.

C. A. MILLER, M.D., Thedford, Neb.

ANSWER.—It is quite possible that the case described is sensitive to heat or effort or to cold. The condition is described in the February issue of the *Archives of Internal Medicine* under the heading Heat and Effort Sensitiveness and Cold Sensitiveness. The patient can be tested objectively by exposing him to a large nitrogen lamp until his skin is hot and later to cold by rubbing him from head to foot rapidly with ice. If either heat or cold augments the itching, a positive diagnosis of heat or cold sensitiveness can be made. The case can probably be successfully treated through the repeated alternations of hot and cold application.

ABSORPTION OF DEXTROSE—HYPODERMOCLYSIS

To the Editor:—1. In THE JOURNAL, July 12, appeared the query "Is there any authoritative opinion on the rate of absorption and the change in blood sugar concentration following dextrose by rectum and by hypodermoclysis?" I wonder whether in making his reply the editor fully considered the article by McNealy and Willems (Surg. Gynec. Obst. **49**: 794 [Dec.] 1929), wherein a plausible conclusion is reached that dextrose is not absorbed by the rectum or the colon. I would appreciate further opinion on this topic in that rectal feedings of dextrose are practiced so frequently and so much faith is held in their nutritional value. I myself am inclined to believe with McNealy and Willems. 2. There has been considerable discussion lately in our circle as to the wisdom of hypodermoclysis given in the thighs in preference to the subpectoral insertion. This area used almost exclusively by our group has temporarily been given up because of two instances of sloughing following the clysis, whereas sloughing following a subpectoral hypodermoclysis has never occurred. I would appreciate your opinion in the matter both as to the region of choice and as to the probable explanation for the sloughing. At present we are considering three factors as probably responsible: (*a*) a hypertonic solution; (*b*) too rapid instillation; (*c*) too concentrated a solution of iodine in preparing the field. 3. Is there any contraindication for giving dextrose 5 per cent in physiologic solution of sodium chloride either as a hypodermoclysis or intravenously? Please omit name.

M.D., Connecticut.

ANSWER.—1. The observations of McNealy and Willems might well explain the generally contradictory evidence available from the literature. It may well be that those observers who secured evidence of absorption or of antiketonic action from rectal administration of dextrose employed a technic that forced the material past the ileocecal valve.

2. Injection in the thigh does not seem to be as well borne as injection into the looser and larger subcutaneous tissue

space of the front of the trunk. Infections, even with gas bacillus and tetanus, seem to occur with greater frequency in thigh injections than elsewhere. Possibly distention in this region interferes with local nutrition more than in the subpectoral region.

3. Dropsy, pulmonary edema and marked cardiac insufficiency are definite contraindications to voluminous subcutaneous or vein infusion.

FLUCTUATION IN SUGAR TOLERANCE

To the Editor:—A 60 year old patient of mine had to maintain a very strict diet to keep free from sugar. I was quite surprised to find that the urine was sugar free and that he had been eating "everything" and feeling fine after taking "Glucosin." Kindly give me your comments on the remedy mentioned. Please omit name and town.

M.D., New York.

ANSWER.—The proprietary preparation mentioned is probably without any value whatever. The result noted is evidently due to a natural fluctuation in sugar tolerance. An infection might have temporarily lowered the patient's sugar tolerance, which improved on his recovery from his infection. Profound emotional disturbance will temporarily lower sugar tolerance. On the other hand, suitable strict dieting may raise the sugar tolerance; and any remedy used afterward might erroneously be given credit for a result that had been achieved by the previous treatment.

ASPERMIA AND AZOOSPERMIA

To the Editor:—In Queries and Minor Notes (THE JOURNAL, August 30, p. 683) you use the term "aspermia" to designate the absence of sperma from the seminal secretion. In the case referred to, the semen was examined and no sperma found. The usual designation of this condition is "azoospermia," meaning the absence of sperma. "Aspermia" is used to signify an absence of ejaculation. It is true that the two terms are often used interchangeably to designate the absence of sperma from the semen, but both cannot be correct. Will you kindly explain your use of "aspermia"? Do you consider this the correct term, as against "azoospermia?" And if so, when would you use the latter term?

A. L. WOLBARST, M.D., New York.

ANSWER.—The editor erred in the title placed on the question referred to and also in the use of the term in the answer. General usage tends to confirm the point of view of Dr. Wolbarst to the effect that aspermia signifies an absence of ejaculation or deficient secretion of semen and that azoospermia indicates an absence of sperm and a lack of spermatozoa in the semen.

CARMINATIVE ACTION OF ONION

To the Editor:—Recently I have heard of, and in fact seen, the following "home remedy" used and apparently work as well as paregoric in preventing young infants from crying and fretting. Can you give me any explanation as to the mode of action, the vegetable compound involved, or any injurious results from giving infants a few drops of the following concoction: Slice an onion thin, place it in a glass dish and sprinkle a thin layer of vinegar over it. Leave for twenty-four hours, and give the resulting fluid in 2-3 drop doses. It makes a child sleep and seems to cause no trouble.

WILLIAM C. HOLT, M.D., Angleton, Texas.

ANSWER.—The effect observed is probably due to the carminative action which the onion is reputed to have.

DERMATITIS FROM TRINITROPHENOL

To the Editor:—Please inform me as to whether or not there is any specific treatment for the severe dermatitis that occasionally occurs following the use of trinitrophenol, alcohol solution, in abdominal preparation of surgical patients. In 2 cases out of approximately 500 there occurred a rash that spread till it finally covered the entire body, and even invaded the mucous surfaces. It is extremely distressing and does not subside for about ten to twelve days.

W. H. BENNETT, M.D., Lamesa, Texas.

ANSWER.—Trinitrophenol (picric acid) remaining at the point of original application may be removed from the skin by a paste of magnesium carbonate. Otherwise the dermatitis would have to be treated in accordance with the recognized principles of dermatology.

INTRAVENOUS THERAPY

To the Editor:—Please advise me whether there is any advantage in giving cinchophen, sodium salicylate and sodium iodide intravenously instead of by mouth. HARRY H. BOLTON, JR., M.D., Pierce, W. Va.

ANSWER.—Unless special conditions make the intravenous route necessary, the intravenous administration of these drugs is not indicated.

Medical Education, Registration and Hospital Service

COMING EXAMINATIONS

AMERICAN BOARD FOR OPHTHALMIC EXAMINATIONS: Chicago, Oct. 27, 1930. Sec., Dr. William H. Wilder, 122 So. Michigan Blvd., Chicago.

ARKANSAS: Little Rock, Nov. 3, 1930. Basic Science. Sec., Mr. Louis E. Gebauer, Little Rock, Ark. Eclectic Board, Little Rock, Nov. 11 and 12, 1930. Sec., Dr. Claude E. Laws, 803½ Garrison Ave., Fort Smith, Ark. Regular, Little Rock, Nov. 11-12, 1930. Sec., Dr. Sam J. Albright, Searcy, Ark. Homeopathic, Eureka Springs, Nov. 11, 1930. Sec., Dr. Allison A. Pringle, Eureka Springs, Ark.

CALIFORNIA: San Francisco and Los Angeles, Dec. 10, 1930. Reciprocity examinations. Sec., Dr. C. B. Pinkham, 420 State Office Bldg., Sacramento, Calif.

CONNECTICUT: Regular, Hartford, Nov. 11 and 12, 1930. Sec., Dr. T. P. Murdock, 147 W. Main St., Meriden, Conn. Homeopathic, New Haven, Nov. 10, 1930. Sec., Dr. E. C. M. Hall, 82 Grand Ave., New Haven, Conn.

FLORIDA: Jacksonville, Nov. 10-11, 1930. Sec., Dr. W. M. Rowlett, P. O. Box 603, Tampa, Fla.

KANSAS: Topeka, Dec. 9, 1930. Sec., Dr. A. S. Ross, Sabetha, Kan.

MAINE: Portland, Nov. 11-12, 1930. Sec., Dr. Adam P. Leighton, 192 State St., Portland, Me.

MARYLAND: Regular, Baltimore, Dec. 9-12, 1930. Sec., Dr. H. M. Fitzhugh, 1211 Cathedral St., Baltimore, Md. Homeopathic, Baltimore, Dec. 9, 1930. Sec., Dr. J. S. Garrison, 517 Old Orchard Rd., Ten Hills, Baltimore, Md.

MASSACHUSETTS: Boston, Nov. 12-14, 1930. Sec., Dr. Frank M. Vaughan, 144 State House, Boston, Mass.

NEBRASKA: Lincoln, Nov. 20-22, 1930. Sec., Mr. Ernest M. Pollard, Lincoln, Neb.

NEVADA: Carson City, Nov. 3-5, 1930. Sec., Dr. Edward E. Hamer, Carson City, Nev.

OHIO: Columbus, Dec. 1-4, 1930. Sec., Dr. H. M. Platter, 85 E. Gay St., Columbus, Ohio.

SOUTH CAROLINA: Columbia, Nov. 11, 1930. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia, S. C.

TEXAS: Waco, Nov. 18-20, 1930. Sec., Dr. T. J. Crowe, 918-19 Mercantile Bank Bldg., Dallas, Texas.

VIRGINIA: Richmond, Dec. 9-12, 1930. Sec., Dr. J. W. Preston, 803 Medical Arts Bldg., Roanoke, Va.

WEST VIRGINIA: Morgantown, Nov. 20, 1930. Sec., Dr. W. T. Henshaw, Charleston, W. Va.

WISCONSIN: Milwaukee, Dec. 13, 1930. Basic Science. Sec., Dr. R. N. Bauer, 3410 Wisconsin Ave., Milwaukee, Wis.

Maryland June Examination

Dr. Henry M. Fitzhugh, secretary of the Board of Medical Examiners of Maryland, reports the written examination held at Baltimore, June 17-20, 1930. The examination covered 9 subjects and included 90 questions. An average of 75 per cent was required to pass. Eighty-eight candidates were examined, 87 of whom passed and 1 failed. The following colleges were represented:

PASSED		
College	Year Grad.	Per Cent
College of Medical Evangelists	(1930)	87.8
Yale University School of Medicine	(1922)	82.3, (1928) 85.8
Georgetown University School of Medicine	(1929)	75.2
George Washington University Medical School	(1930)	84.4, 87.5, 88, 89.6, 91.6, 91.8
University of Illinois College of Medicine	(1930)	89.3
Johns Hopkins University School of Medicine	(1924)	89.5, (1927) 87.1, (1928) 91.8, (1929) 80.1, 83.8, 85, 96.3, (1930) 80.3, 80.5, 81.5, 81.7, 82, 82.1, 82.6, 83, 83.2, 83.3, 84.6, 84.8, 85, 85.4, 86, 86.1, 86.6, 86.8, 88, 88.6, 89, 89, 89.2, 89.4, 89.7, 90.1, 90.5, 91.4, 91.8, 92.5
University of Maryland School of Medicine	(1926) 89, (1927) (1929) 85.8, 90.6, 91.8, (1930) 84.2, 85.6, 86, 86.4 86.5, 87.2, 87.4, 87.5, 87.6, 88, 88.1, 88.3, 88.4, 89, 89.3, 89.6, 89.6, 89.7, 89.8, 90.5, 90.5, 90.6, 91.6, 91.8, 92, 92.2, 92.3, 92.6, 92.7, 93.5	89.5,
Tufts College Medical School	(1928)	85.3
Jefferson Medical College	(1929) 91.3, (1930)	86.4
Temple University School of Medicine	(1929)	85.1

FAILED		
College	Year Grad.	Per Cent
University of Berlin Faculty of Medicine	(1922)	67.8*

Dr. Fitzhugh also reports 13 physicians licensed through reciprocity with other states and 1 by endorsement of National Board credentials. The following colleges were represented:

LICENSED BY RECIPROCITY		
College	Year Grad.	Reciprocity with
College of Medical Evangelists	(1928)	California
University of Colorado School of Medicine	(1906)	Colorado
Georgetown University School of Medicine	(1921), (1926)	Dist. Colum.
George Washington University Medical School	(1927, 2)	Dist. Colum.
National University Medical Dept., Dist. Columbia	(1898)	Wisconsin
Emory University School of Medicine	(1928)	Georgia
University and Bellevue Hospital Medical College	(1900)	New Mexico
Jefferson Medical College	(1913)	Penna.
Medical College of Virginia	(1927)	Virginia
University of Virginia Department of Med.	(1920) (1927)	Virginia

ENDORSEMENT OF CREDENTIALS		
College	Year Grad.	Endorsement of
University of Virginia Department of Medicine	(1924)	N. B. M. Ex.

* Verification of graduation in process.

Book Notices

TREATMENT IN GENERAL PRACTICE. By Harry Beckman, M.D., Professor of Pharmacology at Marquette University, Milwaukee. Cloth. Price, $10 net. Pp. 899. Philadelphia: W. B. Saunders Company, 1930.

Here in book form is the therapeutic index or scrap book that every general practitioner wishes he could prepare and keep for himself. The author has apparently stored in envelops, on cards or by some other indexing method references to most of the important articles on therapeutics that have appeared in medical publications in recent years. He has carefully abstracted and condensed this material and he has used sound editorial judgment in his choice of suggestions that are most worth while. The result is a book on therapeutics that is probably the most practical large book at present available. It is arranged according to diseases of infectious and parasitic causation, allergic disturbances and diseases of the various systems of the body. It includes also intoxications, a special section on burns, obstetrics and a number of miscellaneous subjects.

The material is in practical form for immediate application at the bedside. As with most extensive works of this character, it would seem that the author has distributed the space available occasionally with a desire for elaborateness rather than with a view to the most practical demand for material. The general practitioner will hardly require ten pages on the treatment of leprosy. He could probably use much more on the treatment of measles. He will certainly have little, if any, use for seven pages on plague, but twenty-five to thirty pages on pneumonia are well warranted. Dr. Beckman seems to be somewhat favorably inclined to the Rosenow serum in poliomyelitis, giving it much more space than is devoted to the use of convalescent serum, whereas the latter is much more generally preferred. The treatment of rheumatic fever is, no doubt, a most difficult one and certainly cannot be well handled in four pages. The section on syphilis is fully adequate.

An exceedingly valuable feature of the book is the use of historical and literary quotations preceding the main topics. The author does not hesitate to give exact directions for securing the materials and drugs recommended. Occasionally, his choice of authorities is not what it might be; thus, his section on obesity is taken practically verbatim from Sansum and disregards some of the most important recent contributions to the subject. The section on nervous indigestion is quoted almost wholly from the exceedingly fine contributions of Alvarez. Indeed, there are apparently some ten pages of this quotation. The author is also inclined to follow Alvarez in his treatment of peptic ulcer.

This volume is exactly what is stated in the preface, a collection of excellent abstracts and quotations from the best available literature. It was Josh Billings who said that wit represented a good memory and the ability to choose with judgment. In the same way the preparation of a work on therapeutics of this type represents an organized system for the collection of the best that appears in medical literature, and the ability to reproduce and develop this material in textbook form. In the time that has elapsed since its appearance, the book by Beckman has developed great popularity—a popularity warranted by its practical character and usefulness.

APHORISMES DE MÉDECINE CLINIQUE. Par le Baron Corvisart. Recueillis par F.-V. Mérat. Publiés par le Docteur Paul Busquet, bibliothécaire de l'Académie de médecine. Paper. Price, 20 francs. Pp. 115. Paris: Masson & Cie, 1929.

Corvisart, Napoleon's physician, was not a prolific writer. He is known especially because of his valuable volume on diseases of the heart, and because he translated and brought to the attention of the medical world Avenbrugger's treatise on percussion. Yet he was a leader and pioneer in clinical medicine in Paris, with a great influence on such men as Laënnec through his emphasis on the importance of careful observation with necropsy control. He was a forceful teacher and was fond of epigrammatic statements. Many of these, collected by Mérat, chief of staff of the faculty of Paris, are now for the first time published, with comments, by Busquet. They are well worth reading. Some have naturally lost their point through later discoveries as to the nature of certain diseases, but many of his apothegms are as true today as they were a century ago. From his first to his last, number 324, the interest is maintained. The first: "Medicine is not the art of curing diseases; it is the art of treating them." The three hundred and twenty-fourth: "Purple digitalis, proposed as a remedy against phthisis and dropsy and especially as a drug for lessening the frequency of the pulse, has, in my experience, been successful only once in about seven trials. That was in a case in which it slowed the pulse."

THE NORMAL DIET: A SIMPLE STATEMENT OF THE FUNDAMENTAL PRINCIPLES OF DIET FOR THE MUTUAL USE OF PHYSICIANS AND PATIENTS. By W. D. Sansum, M.S., M.D., F.A.C.P., Director of the Potter Metabolic Clinic, Department of Metabolism, Santa Barbara Cottage Hospital, Santa Barbara, California. Third edition. Cloth. Price, $1.50. Pp. 134. St. Louis: C. V. Mosby Company, 1930.

The author of this work lives in California and he displays a strong preference for such products as oranges, lemons, grapefruit and beans. The book has been quoted extensively and pushed vigorously by the California Fruit Growers Exchange Campaign. The author believes that fully one half of the sickness that has come under his observation has been due, either directly or indirectly, to the elimination of the bulky foods from the diet. He states that the average constipated person requires approximately two pounds of the residue-containing foods daily to insure natural bowel movements and he has his office patients weigh and record the bulky foods. He considers acidosis from an overbalance of the acid-ash foods a great danger. He says: "The living body is always slightly alkaline. If the tissues of the body become acid to the slightest degree, death occurs, and serious illness results long before the alkalinity of the body is reduced to the neutral point. The more common symptoms of the acid-ash type of acidosis are malaise, lassitude, nausea and later vomiting, loss of appetite, headaches, weakness, sleeplessness, muscle aches, acid mouth, sour stomach, acid urine, acid sweat, 'sour disposition,' and, I believe, the blood vessel disease which is responsible for high blood pressure and such complications as partial blindness, heart disease, kidney disease, gangrene and apoplexy." He does not say just how acid the body must be to produce these symptoms but he does state that serious degrees of acidosis may be produced by eating too much bread and meat and that a urine which is acid enough to turn blue litmus paper to red is far too acid and a urine which is alkaline enough to change red litmus paper to blue is probably too alkaline.

The little book by its misstatements seems continually to twist truths to make them support the alkaline-ash, high-residue fad. For example, the author groups cascara, rhubarb, phenolphthalein and castor oil with "the concentrated vegetable and mineral irritants" which "act upon the inner lining of the stomach and bowel in the same manner as an irritating substance affects the eye which 'waters' when such a substance comes in contact with the conjunctiva. . . . And it is the 'tears' on a large scale which produce the copious, unnatural, watery bowel movements." His knowledge of the science of nutrition seems to be weak, for he speaks of proteins as the chief sources of muscular energy. Thus the woman shopper gets a headache long before noon because she does not eat a large breakfast. She has consumed her own fat and so much of her own protein that its acid-ash has caused an acidosis. Benedict's fasting artist, Levanzin, managed to starve for thirty-one days without increasing his protein metabolism above the normal level, but Sansum's shopper apparently could not last half a day. He makes another remarkable statement about a football game: "Whereas 3,500 calories per day is sufficient for a man doing average work, and 5,500 calories is the army ration, our college football players often use up 8,000 calories during the game. They enter such games without food or with a very light lunch. Their energy comes from the burning of their own lean meat, and the more muscular they are the more endurance they seem to have." It is a simple matter to calculate the result of such a football contest. Lean beef round furnishes 512 calories a pound and therefore Sansum's athlete would lose in the course of the game 15 9/10 pounds of muscle. He would have to eliminate approximately twenty times as much urea as the ordinary man does in a

whole day and this would require about 5 or 10 pounds of urine over and above the amount of water furnished by the breakdown of this muscle tissue. Now Benedict and Joslin calculate that a football player in a hard game loses about 13 7/10 pounds of water through skin and lungs. This would make Sansum's man lose between 34 and 39 pounds of weight in the course of little over an hour. Sansum does not explain just why a football player expends from thirteen to fourteen times as much energy per hour as bicycle riders on a century run or swimmers or mountain climbers. A textbook of physiology would give him the figures and any good textbook written during the last two generations would tell him that physical exercise causes practically no increase in the protein metabolism.

The book is of some service in that it emphasizes the value of plenty of water in the treatment of fevers and demonstrates to the public the fact that orange juice and lemon juice act as alkalis when metabolized. On the whole, its biased point of view makes one doubt the extent to which it should be trusted.

DIE BETRACHTUNG UND BETASTUNG (INSPEKTION UND PALPATION) DES BRUSTKORBS BEI LUNGENKRANKEN. Klinische Untersuchungen über diagnostisch wichtige Erscheinungen am Knochengerüst, an Muskeln und Haut, sowie am Nerven- und Gefässsystem des Brustkorbs, mit besonderer Berücksichtigung halbseitiger Veränderungen. Von Oberarzt Dr. J. E. Kayser-Petersen, leitendem Arzt der Tuberkulose-Fürsogestelle für den Stadtkreis an der medizinischen Universitäts-Poliklinik. Paper. Price, 21 marks. Pp. 213, with 39 illustrations. Leipzig: Johann Ambrosius Barth, 1930.

Physicians are so accustomed in examining the chest for pulmonary disease to rely largely on percussion and auscultation, and the x-rays that they overlook the many aids furnished by inspection and palpation. It is enlightening to read such a book as this one and to see how much information is afforded by the use of the eyes and the fingers. Slight deformities, asymmetry, loss of motion, change of color, points of tenderness and change in muscle tension may be mentioned as examples, each with its possible significance as to underlying disease. There are several useful diagrams with brief case histories, together with the roentgen and auscultatory observations. The book is stimulating and timely. It will help call attention to the fact that careful physical examination is still of use and should not be displaced entirely by the laboratory or instrument of precision.

DISEASES OF THE URINARY TRACT IN CHILDREN. By Edwin Beer, M.D., and Abraham Hyman, M.D. Cloth. Price, $6. Pp. 318, with 50 illustrations. New York: Paul B. Hoeber, Inc., 1930.

The authors base their work on twenty years' experience with diseases of the genito-urinary tract in children. The preliminary chapter is devoted to the symptomatology of genito-urinary disease in young life. The technic of cystoscopy and pyelo-ureterography is discussed in some detail. Intravenous pyelography by the use of sodium-2-oxo-5-iodo-pyridine-n-acetate is described and its advantages and indications are pointed out. The use of the Bucky diaphragm is not advised. Edwin Beer writes on enuresis in childhood. He emphasizes the need for a thorough examination in order to determine the etiologic factor. Hyman writes the important chapter on infections of the urinary tract (cystitis, pyelitis, pyelonephritis). He presents the most recent contributions to bacteriologic, experimental, surgical, cystoscopic and roentgenographic progress. He appropriately avers that "pyelitis" is a misnomer which covers a number of conditions, and that "pyuria" is more applicable until the true nature of the underlying lesion is understood. He observes that a large proportion of the chronic pyurias in children, formerly diagnosed as pyelitis, are secondary to urinary stasis due to a congenital anomaly. The author believes that too much emphasis has been placed on the hematogenous theory of kidney infection. He thinks that, of all the predisposing factors favoring infection, urinary stasis and a diminished resistance are the most important. An uncomplicated pyelitis seldom exists; accompanying lesions are found in the kidney in most necropsy specimens. The author notes that persistence of infection is due to lowered immunity, to a calculus in the kidney or ureter, to a persistent suppurative focus somewhere else in the body, or to a urinary stasis caused by a congenital anomaly. Edwin Beer discusses abscess and carbuncle of the kidney. He notes that in cases of cortical abscess in which the symptoms have subsided and diagnosis is difficult, activation of the focus by injecting *Staphylococcus aureus* vaccine in a dosage of from 100 million to 500 million acts as a provocative test and accentuates the clinical manifestations. He points out, as an important radiographic sign in the diagnosis of perinephric abscess, the obscuring of the outer border of the psoas muscle and curvature of the spine to the opposite side. Edwin Beer contributes a chapter on injuries of the kidney and ureter. He notes that the most striking symptoms are hematuria, local pain, local tumor and more or less shock with bleeding as shown by the fall in the hemoglobin of the blood. He advises that in observing these cases of injury to the kidney and ureter one should see every voided specimen of urine and use a rack of test tubes. It can thus be seen at a glance whether the bleeding is ceasing or continuing. Instrumentation may lead to infection and the author considers it contraindicated except when the diagnosis is in doubt. Beer writes the chapter on chronic tuberculosis of the kidney. He states that the all important examinations are urinary and cystoscopic. However, he cautions that in renal tuberculosis pyelography should be the diagnostic method of last resort. The resulting trauma may produce generalized tuberculosis. Hyman considers malignant tumors of the kidney and believes that the most frequent type is the mixed embryonic tumor. This monograph presents the essential clinical and special urologic data in a clear, practical manner. Each chapter is concluded by a group of illustrative case records and a special bibliography. There are numerous instructive roentgenographic reproductions. The volume should be valuable and interesting to pediatricians and urologists.

LE NEUROSI DEL CUORE E DEI VASI SANGUIGNI E LORO CURA. Dal Prof. Giovanni Galli, docente di patologia medica speciale nella R. Università di Pavia. Paper. Price, 50 lire. Pp. 361, with 98 illustrations. Milan: Società Editrice Libraria, 1930.

Galli defines a neurosis as a disease situated in the smaller blood vessels with material lesions that are physical or chemical, as a rule entirely reparable, leaving no anatomic residue. A neurosis is in close relation with the psyche and gives rise to many subjective and objective manifestations that vary according to the organ or the part in which the circulatory disturbance takes place. All through the work while physical, chemical, toxic and other causes are recognized, the stress is laid on psychic influences. There is nearly as much discussion of psychology as of cardiology and neurology. The topics considered are such as tachycardia of various types, extrasystole, palpitation, the nervous heart, respiratory arrhythmia in the circulatory neuroses, hypotension and hypertension on a nervous basis, visceral vasomotor syndromes, vasomotor syndromes of the skin and joints, circulatory neuroses on a sexual basis, psychoanalysis and moral guidance. Not the least interesting and stimulating of his chapters are the earlier ones that are largely historical. The author rarely goes to extremes in his views. He seems possessed of plenty of common sense. Thus while recognizing the value of freudian psychoanalysis he makes it plain that he is not a "pansexualist." His therapy is likewise sound though with a greater faith in drugs than one would expect from his emphasis on the mental features of these neuroses. Galli is a loyal Italian. Exophthalmic goiter is with him Flajani's disease. He also refers to the Morgagni-Adams-Stokes syndrome. There are numerous figures showing polygraphic tracings but none showing electrocardiograms. A new font of type and a little more care in proofreading would have improved the looks of the pages. These, however, are minor criticisms. All in all the book is to be praised as a serious and helpful contribution to the better knowledge and handling of a group of ailments as yet none too well understood.

BURNS: TYPES, PATHOLOGY AND MANAGEMENT. By George T. Pack, B.S., M.D., and A. Hobson Davis, B.S., M.D., Instructor in Pathology, University of Alabama. Cloth. Price, $6. Pp. 364, with 60 illustrations. Philadelphia: J. B. Lippincott Company, 1930.

The authors of this volume are to be congratulated on the masterly manner in which the subject of burns is presented. This excellent treatise is not a mere compilation of data but an amalgamation of a critical selection of the best in the literature with the results of a wide clinical experience. The preface states: "In the preparation of this manuscript, we have included not only our personal experiences, but also a free analysis of the contributions and opinions of other clinicians and investiga-

tors." The senior author was initiated into the management of burns by the incidence of a theater fire in New Haven in 1921 and since then has been associated with a second similar disaster and with the study of many individual cases. This experience has given to him an authority seldom encountered. The book is divided into three parts. Part one contains fundamental facts concerning burns and scalds. The historical aspects of the subject are presented together with a discussion of the etiology, incidence, classification, pathology and cause of death. In part two, consideration is given to the management of thermal burns. Particularly important is the chapter on the character of the immediate treatment of the burned patient and the emphasis laid on the necessity of systemic treatment. "It is the physician's duty to treat the patient as well as the burn and by supportive systemic therapy obviate any visceral mischief and malnourishment." Local treatment of the injury is given a duly prominent position and is discussed from many points of view. The relative merits of various procedures, such as wet dressings, water bath treatment, sunlight therapy and occlusive dressings (paraffin, oils, ointments and powders) are indicated. The technic of skin grafting, the diseases of cicatrices following burns and the prevention and correction of subsequent deformities are critically reviewed and preferred methods selected. In part three, regional burns by specific agents are discussed. This includes burns by such agents as electricity, lightning, roentgen rays, radium, the sun, caustic chemicals and the war gases. The final chapter presents the medicolegal aspects of burns and scalds. There are adequate references to the literature at the end of each chapter, and both subject and author indexes are given. The text is brief, clear cut and decisive. A perusal of this volume gives the feeling that in the present stage of knowledge little can be added to this presentation of burns and nothing can be deleted.

ALLEN'S COMMERCIAL ORGANIC ANALYSIS. A TREATISE ON THE PROPERTIES, MODES OF ANALYSIS, AND PROXIMATE ANALYTICAL EXAMINATION OF THE VARIOUS ORGANIC CHEMICALS AND PRODUCTS EMPLOYED IN THE ARTS, MANUFACTURES, MEDICINE, ETC. With Concise Methods for the Detection and Estimation of Their Impurities, Adulterations, and Products of Decomposition. Volume VIII: Glucosides, Non-Glucosidal Bitter Principles, Enzymes, Putrefaction Bases, Animal Bases, Animal Acids, the Cyanogen Compounds, the Proteins, the Digestion Products of Proteins. Edited by C. Ainsworth Mitchell, M.A., D.Sc., F.I.C. Fifth edition. Cloth. Price, $7.50. Pp. 761, with illustrations. Philadelphia: P. Blakiston's Son & Company, Inc., 1930.

This volume has been entirely rearranged, revised and in some instances partially rewritten. The scope of the book is broad. It contains ten sections, which have been prepared by different authors or co-authors, except three, these being written by the same writer. The sections are on glucosides, non-glucosidal bitter principles, enzymes, putrefaction bases, animal bases, animal acids, the cyanogen compounds, the proteins, and the digestion products of the proteins. An excellent bibliography is given at the end of each section. The authors are to be commended, as the material is well chosen, maintaining the high character of the previous editions. The book should prove useful as a work of reference to the chemist in general and helpful to those working in the realm of laboratory medicine.

NAISSANCE VIE ET MORT DES MALADIES INFECTIEUSES. Par Charles Nicolle, directeur de l'Institut Pasteur de Tunis. Paper. Price, 15 francs. Pp. 218. Paris: Félix Alcan, 1930.

Charles Nicolle is a great investigator in the field of infectious diseases. In 1928 he was awarded the Nobel prize in medicine for his work on typhus fever. He played a decisive part in the demonstration of the value of convalescent serum, notably in typhus. In this book, which is one of a series on various scientific subjects, are discussed fundamental questions of a general nature and of general interest concerning the evolution of infectious diseases. The preliminary chapter deals with the infectious microbes and their modes of action. Then follow chapters on (1) the life and characteristics of the infectious diseases as seen in the individual and in epidemics; (2) on the birth or development of infectious diseases, and (3) on the death or disappearance of these diseases as the result of the spontaneous workings of natural forces and of human efforts. The discussion is along rather broad lines. Facts, theories and speculations are presented lucidly without any undue claims of finality for the conclusions that are advanced tentatively. Contrary to the results of recent historical studies, the so-called American origin of syphilis is taken for granted without question. The book will interest educated persons and to physicians and medical workers it will be a stimulus toward a clearer understanding of infectious diseases in their broader biologic aspects.

PHYSIOLOGICAL PRINCIPLES IN TREATMENT. By W. Langdon Brown, M.A., M.D., F.R.C.P., Physician to St. Bartholomew's Hospital. With the collaboration of R. Hilton, M.A., M.B., M.R.C.P., Assistant Physician and Assistant Director of the Medical Unit, St. Bartholomew's Hospital. Cloth. Price, $3.75 net. Pp. 464. New York: William Wood & Company, 1930.

In this age of progressively accelerated progress, books of this kind are a necessity; and every practicing physician owes it to himself and his patients to keep his concepts on physiology from growing stale by reading a book like this once every few years. Even the young physician, out of medical school but a few years, will be surprised at the rapidity with which physiology is outgrowing his notions acquired in school. The perusal of this book makes one wish for the time to return when clinicians were teachers of physiology. Courses on pure physiology given by nonmedical men should be relegated to the premedical studies. A vigorous course on applied physiology should be an essential factor of every medical course worthy of its name: for the practice of medicine is largely applied physiology. In therapeutic suggestions, this book is a veritable gold mine. Here are a few of the nuggets: "The administration of thyroid extract diminishes the amount of bile salts in the urine with great relief of pruritus" in cases of jaundice. "In hematemesis . . . I place considerable reliance on half drachm doses of the 1:1,000 solution of adrenalin chloride in half an ounce of water every three to four hours. In addition to constricting the bleeding point it stops peristalsis." "It will often check vomiting or hiccup in doses of 10 to 15 minims of a 1:1,000 solution diluted with water. I have found this most useful in combination with 1 minim of carbolic acid and 3 minims of dilute hydrocyanic acid." "Corpus luteum hormone . . . inhibits ovarian secretion between oestra and particularly during pregnancy. . . . We have seen it successfully used in the prevention of habitual abortion." "In hypochlorhydria . . . the combined use of alkalis before meals, followed after meals by a good dose of dilute hydrochloric or nitrohydrochloric acid with nux vomica, has given me more satisfactory results than either separately. And we should not be niggardly; for even the full pharmacopeial dose of 20 minims would only confer an acidity of 0.02 per cent on a pint of fluid. . . . In complete achlorhydria up to a drachm of dilute hydrochloric acid in a half pint of lemonade or orangeade should be given during meals." "Fifteen grains of calcium lactate three times a day in water should control functional albuminuria." "Lactose in doses of from 2 to 4 drachms three times a day in hot water before meals often achives the same end as *Bacillus acidophilus* and may do away with the need for aperients. As to the selection of cases, the treatment can only be expected to be beneficial where there is definite evidence of increased putrefaction of proteins. The reaction of the feces will be a guide; if they are acid, this treatment is unsuitable; if they are alkaline at first, but yield a fair quantity of gas in the fermentation tube, showing an acid reaction after, the treatment will probably be unsuccessful. Good results can only be expected in cases where the fresh feces are alkaline and remain alkaline after twenty-four hours, yielding hardly any gas to the fermentation tube."

DIE ZENTRALE ABSTIMMUNG DER SEHSPHÄRE. Von Dr. Hans Hoff, Abteilungsassistent der Klinik. Paper. Price, 7.80 marks. Pp. 96, with 7 illustrations. Berlin: S. Karger, 1930.

This short brochure, which is number 54 of the Abhandlung aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebieten, deals with clinical, experimental and deductive evidence of the influence of adjacent centers on the visual cortical region. There are ten chapters which vary from the influence of sleep on vision and vice versa to a consideration of the genesis of optical hallucinations. Seventeen cases are used to illustrate various points and, most remarkable to state, not once is there a dream analysis based on sex stuff. The deductions from the experimental work seem somewhat exaggerated to the clinician, for the analysis of subjective canine functions depends for the greatest extent on the analyzer and not the canine. Again, some of the analyses of the so-called visual field scotomas lead

an ophthalmologist to believe that the author would be a help in developing the account of a piscatorial excursion into the northern woods (vide page 28). The concluding chapter, which deals with the psychophysical variations in the functional regions of the occipital cortex, is well worth while.

Medicolegal

Lumbago or Sacro-Iliac Strain

(Taylor v. Southern Engineering Const. Co. (La.), 125 So. 877)

Taylor was working on a pile driver, in the construction of a bridge. He accidentally fell from 15 to 25 feet into the water, striking on his back, swam and waded out of the stream, and walked several hundred yards to the tent where he slept. He went home the following day, after doing a day's work. There he was confined to his bed for two weeks or more and partly confined there for three or four months. Prior to the fall, the patient had been engaged in heavy manual labor and had not complained of his back. After the accident and up to the time of the trial, nearly eighteen months, the patient worked only two days immediately following the accident and about five and one-half days on another job. He had to give up the latter work because it caused him so much pain.

The patient's employer, the Southern Engineering Construction Company, the defendant in this case, paid compensation under the employers' liability act from the date of the accident up to June 18, 1928, but paid nothing thereafter. The patient thereupon brought suit, claiming compensation for total disability. In the Eighth Judicial District Court, Parish of Grant, judgment was given in the patient's favor. His employer then appealed to the Court of Appeal of Louisiana, Second Circuit.

Dr. J. I. Peters, who examined the patient for the employer's insurer, testified in the course of the trial that in January, 1929, he was led by an examination of the patient and reports of inspectors to believe that the plaintiff was faking injury. He examined the patient again in June, 1929, assisted by Dr. D. C. McBride, and the roentgen ray showed no evidence of injury. If the patient was then suffering from pain, it was plainly caused by lumbago, "due to other pathological causes quite as much, if not more, than the injury." Dr. Peters based this conclusion on the roentgen examination, which showed an anomaly of the spine, together with the fact that the patient had sources of septic infection, diseased tonsils and teeth. The witness would not say that it was impossible for a patient to suffer a severe sprain of the sacro-iliac joint, sufficient to incapacitate him, without there being some bony injury, or some separation of bony relations, or some callus formation from bony injury, discoverable later by the roentgen ray, but he thought it improbable that such an injury could exist without some of these conditions being discoverable.

Dr. D. C. McBride, who assisted Dr. Peters in his second examination, in June, 1929, testified that the examination showed some stiffness in the lower part of the patient's back and that the patient complained of pain over the sacro-iliac region and the crest of the ilium. He manifested some difficulty in completely flexing or extending the thighs and was limited in flexion, extension and rotation of his spine. Dr. McBride concluded that the patient was suffering from some impairment in the sacro-iliac region, but he believed the trouble was due to absorption from some source of infection and that the plaintiff's teeth and tonsils could cause the trouble. He found no evidence of injury. The anomalous condition of the patient's vertebra may have exaggerated conditions. The fall may have been the beginning of the trouble, which the points of infection continued. It was probable that the patient's injury had something to do with his present condition. Any part that is injured, especially joints, tends to be a point of infection. Dr. McBride thought that the patient would be able to do hard manual labor, if his tonsils and teeth were removed.

Dr. Rand testified that the patient had a definite sacro-iliac strain; it would have been remarkable for the plaintiff to have described the symptoms if he had not had them. A roentgen examination would not necessarily show such an injury as the patient complained of, because of the peculiar, irregular-shaped joint; the plane between the sacrum and the ilium is not a flat surface but is curved. Dr. Rand had had patients in whom the roentgen ray indicated a normal condition, notwithstanding the fact that there was a strain of the sacro-iliac joint.

Dr. M. Cappel had examined the patient twice. The roentgen examination showed an abnormal formation of the sixth [sic] lumbar vertebra, and a back so formed was more susceptible to injury than a normal back. A person, Dr. Cappel testified, can sustain a severe injury to the muscles, ligaments and nerves of the back, without a roentgen examination showing it. He was positive that the patient was suffering from a sacro-iliac sprain. The patient, according to Dr. Cappel, was not suffering from bad tonsils or bad teeth. He was suffering from a disability that made it painful to perform manual labor.

The Court of Appeal pointed out that while Dr. Peters and Dr. McBride, who examined the patient on behalf of the employer's insurer, contended that the patient's trouble was due to his infected teeth and tonsils, they were not willing to say that the injury received by the patient when he fell was not a contributing factor to his present condition, and the court added:

> "The compensation paid injured workmen under the compensation staute is based upon disability and it is immaterial whether the injury alone, or in conjunction with a latent systemic infection, caused the disability."—*Womack v. New Orleans Public Service, Inc., 5 La. App. 71.*

Dr. Peters and Dr. Meyers and other doctors who testified for the employer, said the Court of Appeal, contended that a sprain as severe as the one claimed by the plaintiff almost always causes a widening of the bony relation, or other bony injury, that will be shown by the roentgen ray. But Dr. Cappel and other physicians who testified for the patient denied that statement and cited cases they had treated in which the injury of the sacro-iliac joint was so severe as to cause total disability for several years and in which the roentgen ray showed nothing. Positive testimony will prevail over negative. When a physician, testifying as a medical expert, gives his professional opinion to the effect that a sprain of the sacro-iliac joint, severe enough to cause total disability, will not necessarily cause a widening of the bony relations or other bone injury sufficient to show in roentgenograms and declares that he is treating numerous cases of that kind in which nothing is shown by the roentgen ray, his testimony must prevail over that of another medical expert who expresses the opinion that such a sprain will always show in the roentgen picture.

The patient in this case, concluded the Court of Appeal, is a man of average ability and learning. He has never performed any work other than manual labor and is totally disabled for such work. He therefore comes under the total disability clause of the workmen's compensation law. The judgment of the district court was therefore amended by increasing the amount allowed the patient so as to compensate him on the basis of total disability, and the judgment as thus amended was affirmed.

Society Proceedings

COMING MEETINGS

American Academy of Ophthalmology and Otolaryngology, Chicago, October 27-31. Dr. W. P. Wherry, Medical Arts Building, Omaha, Secretary.

American Academy of Physical Therapy, Boston, November 12-14. Dr. Thomas L. Smyth, 111 North Eighth Street, Allentown, Pa., Secretary.

American Association of Railway Surgeons, Chicago, November 5-7. Dr. Louis J. Mitchell, 29 East Madison Street, Chicago, Secretary.

American Public Health Association, Fort Worth, Texas, October 27-31. Mr. Homer N. Calver, 370 Seventh Avenue, New York, Executive Secretary.

Central States Pediatric Society, Memphis, Tenn., November 7-8. Dr. A. H. Parmelee, 310 South Michigan Boulevard, Chicago, Secretary.

Medical and Surgical Association of the Southwest, El Paso, Texas, November 6-8. Dr. W. Warner Watkins, Box 1587, Phoenix, Ariz., Secretary.

Radiological Society of North America, Los Angeles, December 1-5. Dr. I. S. Trostler, 25 East Washington Street, Chicago, Secretary.

Southern Medical Association, Louisville, Ky., November 11-14. Mr. C. P. Loranz, Empire Building, Birmingham, Ala., Secretary.

Southern Surgical Association, Lexington, Ky., December 9-12. Dr. Robert L. Payne, 142 York Street, Norfolk, Va., Secretary.

Western Surgical Association, Kansas City, Mo., December 5-6. Dr. Frank R. Teachenor, 306 E. Twelfth St., Kansas City, Mo., Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers to THE JOURNAL in continental United States and Canada for a period of three days. Issues of periodicals are kept on file for a period of five years only. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending, but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American J. Medical Sciences, Philadelphia

180: 305-452 (Sept.) 1930

*Etiologic Relationship of Achylia Gastrica to Pernicious Anemia. W. B. Castle, W. C. Townsend and C. W. Heath, Boston.—p. 305.
*Normal Filament and Nonfilament Polymorphonuclear Neutrophil Count: Practical Value as Diagnostic Aid. D. L. Farley, H. St. Clair and J. A. Reisinger, Philadelphia.—p. 336.
*Diagnosis of Pneumococcus Peritonitis from Blood Picture. C. L. Gibson, New York.—p. 344.
*Digitalis Therapy in Lobar Pneumonia. W. L. Niles and J. Wyckoff, New York.—p. 348.
*Barium Chloride in Stokes-Adams Syndrome of Complete Heart Block. A. E. Parsonnet, Newark, N. J., and A. S. Hyman, New York.—p. 356.
*Uninfected Mural Thrombi of Heart. E. A. Harvey and S. A. Levine, Boston.—p. 365.
Flarimeter Tests of Circulatory Fitness. L. F. MacKenzie, P. V. Wells, E. C. Dewis and L. S. Ylvisaker, Newark, N. J.—p. 372.
*Production of Hypertrophic Arthritis by Interference with Blood Supply. A. D. Goldhaft, L. M. Wright and R. Pemberton, Philadelphia.—p. 386.
*Subphrenic Abscess. Gatewood, Chicago.—p. 398.
*Remote Symptoms of Unrecognized Thyroid Adenomata. P. K. Gilman and W. E. Kay, San Francisco.—p. 405.
*Anorexia Nervosa, Anorexia, Inanition and Low Basal Metabolic Rate. J. M. Berkman, Rochester, Minn.—p. 411.

Relationship of Achylia Gastrica to Pernicious Anemia.—Experiments were performed by Castle et al. to test the validity of the hypothesis that the genesis of the disease pernicious anemia is dependent on an inadequate gastric digestion of protein, thus permitting the development of a virtual deficiency in the presence of a diet adequate for the normal individual. They conclude that the active constituent (intrinsic factor) of the normal human fasting gastric contents is in all probability secreted by the mucosa of the stomach and is not detectably present in normal saliva or duodenal contents free from gastric juice, or in the secretions of any portion of the gastro-intestinal tract of the patient having pernicious anemia. This substance is probably organic, thermolabile, possibly an enzyme, capable of interaction with protein (extrinsic factor) or closely related substances in neutral solution, resulting in the production of material having, when administered to patients with pernicious anemia, a marked hematopoietic effect. If an enzyme, it is certainly not pepsin; its properties as so far determined are only in certain respects similar to those of rennin. The lack of this particular property (intrinsic factor) of the gastric contents in pernicious anemia is probably the essential defect leading to the development of the disease, through a failure of the normal reaction, occurring in these experiments with beef muscle proteins (extrinsic factor, and normal human gastric juice. It is also concluded that the existing tests for hydrochloric acid and pepsin of the gastric juice are not necessarily of value in determining the presence or absence of the intrinsic factor essential to the reactions between normal human gastric juice and beef muscle described in these papers.

Normal Filament and Nonfilament Polymorphonuclear Neutrophil Count.—Farley et al. are of the opinion that the most delicate method of studying the reaction of the bone marrow in infections of all types is the estimation of the young forms of polymorphonuclear neutrophils. This is in agreement with others. It is especially valuable in the diagnosis of cryptic infections of subacute or chronic types in which there is no increase in the total leukocyte count. It may add additional presumptive evidence in cases of malingering and hysteria masquerading as organic disease. Its value in prognosis is yet to be established. In profoundly toxic cases with a normal total count or a leukopenia, the agonized efforts of the bone marrow can be determined only by study of the character of the nucleus of the leukocyte. Their method is the differentiation of 100 consecutive leukocytes to determine thus the percentage of nonfilament neutrophils, filament neutrophils, lymphocytes, monocytes, eosinophils and basophils, in which Cooke's criterion is used to separate the polymorphonuclear neutrophils into old and young groups. This method is recommended especially for routine clinical examinations and not in competition with the more complex methods available to expert hematologists. The authors have found by this method that the upper limit of a normal young polymorphonuclear leukocyte (nonfilament) count is in the neighborhood of 16 per cent of cells. The average count in 190 presumably normal adults was approximately 8 per cent. An increased percentage of young polymorphonuclear leukocytes may indicate the existence of infection, even though the total number of leukocytes is not increased.

Diagnosis of Pneumococcus Peritonitis from Blood Picture.—In pneumococcic peritonitis, Gibson regards the characteristic picture of an extraordinarily high leukocyte count with high percentage of polymorphonuclears as a valuable point in differential diagnosis from appendical and other nonpneumococcic forms of peritonitis.

Digitalis Therapy in Lobar Pneumonia.—Two years of observation in hundreds of cases has convinced Niles and Wyckoff that the results obtained do not justify continuing the routine administration of digitalis to patients suffering with lobar pneumonia.

Barium Chloride in Stokes-Adams Syndrome of Complete Heart Block.—Parsonnet and Hyman report on their experiences with barium chloride in doses of from 0.04 to 0.6 Gm. daily in eight cases of auricular and ventricular dissociation exhibiting the Stokes-Adams syndrome. In no case did the barium exert any influence, either good or bad, on the frequency or severity of the seizures, nor was the progress of the myocardial changes altered. In one case barium was administered 126 days and in no case less than 40 days. The total amount of barium taken all together varied from 9.6 to 40.32 Gm.

Uninfected Mural Thrombi of Heart.—Harvey and Levine reviewed 2,091 necropsy records. The incidence of thrombi of the heart was found to be approximately 5.3 per cent, or 111 instances. The frequency of thrombi was slightly greater in the auricles than in the ventricles. The two most common sites of thrombus formation were the tip of the left ventricle and the right auricular appendix. This was true for both isolated and multiple thrombi. Thrombi were found to be slightly more frequent on the left side of the heart than on the right (87 to 72). In analyzing the condition in the auricles and the ventricles separately, however, there was a great predominance in the right auricle as compared to the left (60 to 28) and in the left ventricle as compared to the right (59 to 12). It is apparent from a study of the pathologic finding in these cases that the sequence of coronary artery disease, cardiac infarction and mural thrombosis of the ventricles is the most common mechanism of the production of thrombi in the chambers of the heart. Cardiac mural thrombi were twice as frequent in males as in females. The majority of these patients died between the ages of 40 and 70 years. The patients with ventricular thrombi following cardiac infarction formed the oldest age group (62 years). There was a large middle-aged group with valvular disease (45 years). Secondary infarction outside the heart as a result of emboli occurred with the following frequency: pulmonary, 47; renal, 18; splenic, 12; cerebral, 3 (the brain was examined in only a limited number of instances). There were six instances of peripheral arterial thrombosis that may have been embolic. Auricular fibrillation definitely increases the incidence of auricular thrombosis. The two most frequent mechanisms for the formation of cardiac mural thrombi are the myocardial degeneration associated with coronary arterial disease and the improper functioning of the auricles leading to blood stasis. The diagnosis of cardiac mural thrombosis presents difficulties but should be suspected in cases of coronary thrombosis and chronic valvular disease showing evidence of emboli.

Production of Hypertrophic Arthritis by Interference with Blood Supply.—Experiments are reported by Goldhaft

et al. in which the phenomena of arthritis, chiefly of the hypertrophic variety, are brought about in the region of the patella of dogs by ligation of the blood supply to the patella. Control experiments in which an amount of silk ligature equal to that used in the original experiments was placed around the patella, following on an otherwise essentially identical operation, failed to produce any overgrowth after a comparable lapse of time. Analyses of the overgrowth and of the original patella giving rise to the overgrowth show that the percentage magnesium content in these tissues is higher than on the control side. The involvement of the mineral metabolism in the region affected is thus clearly indicated. These experiments are in entire consonance with those arrived at, following a different line of reasoning, by Wollenberg and indicate beyond any reasonable doubt that disturbance of the blood supply must henceforth be regarded as one of the factors capable of producing arthritic change. Taken in conjunction with other work, these experiments afford strong evidence that interference with the blood supply, probably in the nature of vasoconstriction, constitutes at least a part, probably a large part, of the underlying physiologic disturbance productive of the phenomena of chronic arthritis, especially the hypertrophic type as encountered in human beings.

Subphrenic Abscess.—A review of the literature by Gatewood and of forty-one cases observed in the Presbyterian Hospital during the past ten years shows that the mortality in subphrenic abscess is still much too high, being 30 per cent or more. In spite of improved diagnosis methods and earlier operation, acute appendicitis ranks high as an etiologic factor —second in this series. The importance of prophylactic treatment cannot be overemphasized. Early diagnosis of appendical and other contributory causes and their prompt elimination will prevent the formation of many subphrenic abscesses. Adequate drainage and the adoption of the semisitting posture in all lower abdominal infections are two most important preventive measures that should not be forgotten. Finally, attention is again called to the failure to consider the likelihood of subphrenic abscess in any patient not doing well after an abdominal operation, even though performed months previously.

Remote Symptoms of Unrecognized Thyroid Adenomas.—In the thirteen cases reported by Gilman and Kay, the classic signs of thyroid toxicity were for the most part absent. Furthermore, the basal metabolic rate in each instance was either normal or below normal. In many instances the patients were more or less indefinite in their complaints but were unanimous in stating that they did not feel well and knew that something was definitely wrong. Their symptoms largely directed attention away from the thyroid gland and suggested trouble with systems elsewhere in the body. Nervousness was the most frequent symptom. This nervousness was not suggestive of the type usually seen in thyrotoxicosis. It was in the nature of a nervous tension and sense of apprehension, associated with a feeling of carrying too heavy a load. As a rule this symptom was brought out only after careful questioning, thus differing from the objective nervousness usual in hyperthyroidism. Several of these patients had been classified as psychoneurotic, chiefly of the neurasthenic type. Weakness, fatigability and palpitation were common symptoms and present in nearly all the cases. These, with shortness of breath, had evidently led to a previous diagnosis of cardiovascular disease in nearly half of these patients. Five of the thirteen patients exhibited a definite hypertension, three showing a high diastolic pressure and cardiovascular damage. The other two showed definite heart and blood vessel changes but to a lesser degree. Attention was directed especially to the gastro-intestinal tract in three of the patients. One patient had been previously treated for more than a year for gallbladder disease and colitis; a second case, diagnosed as sprue, had been treated for a chronic enteritis for five years. The third had been under treatment for stomach trouble. One patient had had a chronic cough and had been diagnosed as having pulmonary tuberculosis. Among the less frequent symptoms, loss of weight was present twice; dizziness was complained of twice; tremor of the fingers but once. A feeling of warmth was not complained of in any instance in this series. The pulse rate was usually a little increased but seldom over 80 per minute. In two cases the rate was between 60 and 70 per minute. The authors urge that in such case adenomas of the thyroid must be carefully excluded as the underlying cause. Toxic adenomas are not necessarily accompanied by an increased basal metabolic rate but may be present with a normal or subnormal rate. The improvement these patients exhibited following operation was striking and gratifying.

Anorexia Nervosa, Anorexia, Inanition and Low Basal Metabolic Rate.—According to Berkman, anorexia nervosa constitutes a definite clinical entity. Briefly, its clinical characteristics are anorexia, inanition, emaciation, various gastrointestinal disturbances, marked nervous manifestations, and low basal metabolic rate. The condition is not common. At the Mayo Clinic, 117 cases were so diagnosed in thirteen years. It seems probable that the low basal metabolic rate is the result of inanition. The absence of any demonstrable pathologic change characterizes the condition as a physiologic disorder secondary to a psychic disturbance. The reestablishment of normal intake of calories is the direct goal, and to this end treatment with a preparation of thyroid gland has been proved to be a valuable adjunctive measure. A similar condition due to inanition may be found in some cases in the absence of anorexia.

American Journal of Physical Therapy, Chicago

7: 221-264 (Sept.) 1930

Medicolegal Melange. I. S. Trostler, Chicago.—p. 227.
Light Therapy in Cities. E. Biancani and H. Biancani, Paris, France. —p. 231.
Radon Seeds in Treatment of Carcinoma. H. S. Souttar, London, England.—p. 234.
Advantages of Natural Heliotherapy. W. H. Watters, Boston.—p. 245.
Life: An Autonomous Process. O. B. Schellberg, New York.—p. 257.

American J. Roent. & Radium Therapy, New York

24: 225-348 (Sept.) 1930

Mediastinal Pleural Effusion. J. Sagel and L. G. Rigler, Minneapolis. —p. 225.
*Bone Lesions in Tardive Heredosyphilis. E. P. Pendergrass, R. L. Gilman and K. B. Castleton, Philadelphia.—p. 234.
Roentgenologically Demonstrable Changes in Bone in Gaucher's Disease: Case. B. R. Kirklin and H. W. Hefke, Rochester, Minn.—p. 258.
Sarcoma of Rib. R. J. Reeves and H. H. Kasabach, New York.—p. 262.
*Menstrual Headaches. C. L. Martin, Dallas, Texas.—p. 267.
*Ten Years' Results with Radium in Treatment of Toxic Goiter. R. E. Loucks, Detroit.—p. 280.
*Value and Place of Radium in Treatment of Diseases of Thyroid Gland. S. Ginsburg, New York.—p. 283.
Barium Enema Entering Esophagus: Case. C. G. Lyons, Hines, Ill. —p. 300.

Bone Lesions in Tardive Heredosyphilis.—Pendergrass et al. report the case of a man who had almost every possible type of bone involvement found in syphilis, all of which responded to treatment. Cutaneous manifestations, and involvement of the liver and spleen were interesting complications. The patient responded to antisyphilitic therapy and the change produced in the bones is described.

Menstrual Headaches.—Martin asserts that one type of menstrual headache, characterized by pain in the occipital or frontal regions, and nausea and vomiting, and relieved during pregnancy, probably has an endocrine origin. This type of headache may be partially or completely relieved in a certain number of women past the age of 40 by the production of an artificial menopause with irradiation. The use of castration in younger women seems of doubtful value and may even accentuate the symptoms.

Radium in Treatment of Toxic Goiter.—Reviewing the results achieved with radium in the treatment of hyperthyroidism, including the diffuse exophthalmic type as well as that associated with adenoma, Loucks says that they parallel those obtained with surgery; the type of case that responds poorly to irradiation is identical with that which requires two or more thyroid operations. Radium therapy accomplishes a marked restoration of sugar tolerance in cases associated with glycosuria, indicating a complete control of the hyperactive thyroid. The primary mortality is nil; preoperative and postoperative morbidity is eliminated; from the standpoint of the period of disability, hospital expenses and the concomitant loss of wage-earning power, radium holds a tremendous economic advantage over any other therapeutic procedure.

Radium in Treatment of Diseases of Thyroid Gland.—Ginsburg ardently advocates the use of radium in the treatment of benign and malignant diseases of the thyroid. It effects more cures and has a much lower mortality than surgery. In exophthalmic goiter, clinical cure of a lasting kind has been obtained not only by implanting radium interstitially into the thyroid gland but also by external application of properly screened radium. Radium therapy, efficiently used, relieves not only the toxic but also the compression phenomena in toxic adenomatous goiter, or toxic adenoma of the thyroid. Radical surgery has failed to produce permanent cure of thyroid cancer even when the operation was performed in the so-called early stage of the disease. The end-results of surgery in thyroid cancer would justify the method only in the absence of any superior method.

Annals of Otol., Rhinol. and Laryngology, St. Louis.

39: 349-562 (June) 1930

Pathology and Intramural Electrocoagulation of Inferior Turbinate. J. C. Beck, Chicago.—p. 349.
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Surgical Anatomy of Lymphatics of Head and Neck. H. A. Trotter, Buffalo, N. Y.—p. 384.
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Thymus Gland Hypertrophy and Significance to Otolaryngologist. J. A. Fisher, Asbury Park, N. J.—p. 432.
Diagnostic Problem in Orbital Cellulitis. J. A. Babbitt, Philadelphia.—p. 444.
Palatal Palpebral Reflex. C. J. Imperatori, New York.—p. 458.
Psammoma (Brain-Sand Tumor) Removed from Ethmoid and Sphenoid Area. H. M. Goodyear, Cincinnati.—p. 463.
Proteins as They Apply to Ophthalmology and Otorhinolaryngology. S. R. Gifford, Chicago.—p. 468.
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Hyperpyrexia (Fatal) Following Tonsillectomy. S. J. Pearlman and S. Salinger, Chicago.—p. 502.
Allergy and Relation to Inflammatory Diseases of Paranasal Sinuses. F. K. Hansel, St. Louis.—p. 510.
Latent Meningitis Complicating Surgical Mastoiditis; Significance of Headache; Limitation of Pediatrician's Attendance. V. Dabney, Washington, D. C.—p. 527.
Closure of Alveolar Fistula by Scar Tissue Formation. E. P. Weih, Clinton, Iowa.—p. 533.
Accessory Nasal Sinuses: Comparative Morphology of Nasal Cavities of Amphibia. P. R. Nemours, St. Louis.—p. 542.
Tracheotomy. M. C. Myerson, New York.—p. 563.
Plea for More Conservatism in Treatment of Nasal Accessory Sinus Infections. W. W. Carter, New York.—p. 578.
Upper Respiratory Tract as Guide to Nutritional Disasters. D. C. Jarvis, Barre, Vt.—p. 584.
Novocain Applied Topically as Local Anesthetic in Nasal Surgery. E. Neff and W. B. Dimond, Madison, Wis.—p. 593.
Importance of History in Diagnosis of Brain Abscess. F. T. Hill, Waterville, Me.—p. 595.
Bacteriologic and Cytologic Study of Maxillary Antrum in Children. B. J. Ashley and W. V. Frick, Portland, Ore.—p. 605.
Simple Method of Keeping Sinus Roentgen Records. J. A. Pratt, Minneapolis.—p. 634.
Laryngeal Diphtheria. V. K. Hart, Statesville, N. C.—p. 636.

Annals of Surgery, Philadelphia

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*Influence of Hyperthyroidism on Secretion of Free Hydrochloric Acid. A. Brown, Omaha.—p. 321.
*Cardiac Arrest. T. M. Green, Wilmington, N. C.—p. 331.
*Chordotomy for Intractable Pelvic Pain. C. S. Beck, Cleveland.—p. 335.
*Mortality and Late Results of Subtotal Gastrectomy for Radical Cure of Gastric and Duodenal Ulcer. A. A. Berg, New York.—p. 340.
Deformities and Obstructions of Stomach and Duodenum. A. G. Brenizer, Charlotte, N. C.—p. 367.
*End-Results in Five Hundred Cases of Cholecystectomy. R. L. Sanders, Memphis, Tenn.—p. 376.
Inflammation of Meckel's Diverticulum. W. L. Wolfson and M. J. Clurman, New York.—p. 388.
*Surgical Treatment of Urinary Incontinence in Women. M. K. Smith, New York.—p. 394.
Surgical Treatment of Genital Elephantiasis in Male. D. M. Davis, Baltimore.—p. 400.
Torsion of Spermatic Cord in Infancy. E. J. Donovan, New York.—p. 405.
Dependable Method for Suturing Stomach and Intestines. J. L. Yates and F. Raine, Milwaukee, and W. Thalhimer, Chicago.—p. 410.
*Noneffect of Irradiated Ergosterol in Treatment of Fractures. K. M. Lewis, New York.—p. 415.
Intra-Articular Endothelial Tumors Arising from Synovial Membrane. L. C. Wagner, New York.—p. 421.
Multiple Myeloma as Single Lesion. C. F. Geschickter, Baltimore.—p. 425.
*Malignant Tumors and Their Metastases. J. E. McWhorter and A. W. Cloud, New York.—p. 434.
Desmoid Tumors. J. B. Mason, Rochester, Minn.—p. 444.
Hernia of Umbilical Cord (Exomphalos). A. Horwitz, Washington, D. C.—p. 454.

Influence of Hyperthyroidism on Secretion of Free Hydrochloric Acid.—In Brown's opinion the symptoms of hyperthyroidism can be interpreted in terms of an increased sympathetic drive due to the action of the altered thyroid hormone causing an oversensitization of the thoracicolumbar sympathetic system which overrides the normal antagonistic moderator action of the parasympathetic. The drive is present with varying intensity in the different portions of the sympathetic system and the relative preponderance of ocular, cardiac or gastric symptoms depends on the degree to which the various parts of the sympathetic mechanism are affected by the altered thyroid secretion. Interpreted in terms of the secretion of free hydrochloric acid, the increased sympathetic drive causes a stimulation of the inhibitory acid-secreting fibers of the gastric mucosa and results in a diminution or lack of secretion of acid.

Cardiac Arrest.—Green feels that the occurrence of cardiac arrest is perhaps more frequent than physicians are inclined to think. It may be the cause of death in a large majority of the cases that occur on the operating table, whether it is primarily a cardiac failure or cardiac failure secondary to vasomotor relaxation. Primary cardiac arrest can be combated successfully by cardiac massage. Cardiac arrest secondary to vasomotor relaxation can be prevented by preserving the vasomotor tone during the operation and combated by raising the intracoronary tone through intra-arterial injections of fluid followed by intravenous injections of fluid. In this type of arrest, direct cardiac massage may also be of great value. The success of the issue depends, to a large extent, on the preparedness of the operating room to combat such an eventuality.

Chordotomy for Intractable Pelvic Pain.—Beck's patient had sustained a crushed pelvis and a rupture of the bladder. The left ilium, both ischia and the left pubis were fractured. The left transverse process of the fifth lumbar vertebra was also fractured. The patient suffered considerable pain of a dull, boring, constant nature, localized almost entirely between the costal margin on the left and the lower part of the pelvis. In view of the localization of the pain almost entirely to the left side, it was thought that section of the pain fibers on the right side of the cord would give relief. Laminectomy was carried out over the fourth, fifth and sixth thoracic vertebrae. The dentate ligament on the right side of the spinal cord was picked up in a small clamp and the cord rotated to the opposite side. This exposed the anterolateral tract on the right side. The point of a scalpel was inserted just anterior to the dental ligament to a depth of 3.5 mm. and carried forward for about the same distance. The area of anesthesia on the left side of the body was then determined and it was found to be adequate. The operative wound was sutured. The patient immediately felt relieved of the former pain. Convalescence was uneventful. The area rendered anesthetic to pin-point pain extended from the costal margin on the left downward over the pelvis and left leg. The sensation of heat and cold was lost over this area. The sensation of light touch was preserved. The reflexes were normal. The sense of position and the vibratory sense were normal. There was no motor involvement and there was no difficulty in urination.

Results of Subtotal Gastrectomy for Gastric and Duodenal Ulcer.—In 401 primary subtotal gastrectomies for ulcer of the stomach below the cardia or in the duodenum, Berg reports 6.9 per cent mortality. This mortality includes every death following primary subtotal gastrectomy during six years of ward and five years of private service. It includes all bleeding ulcers, active or arrested, all patients with chronic pulmonary lesions, all patients with chronic cardiovascular disease, all patients with tetany and all patients with chronic renal lesions. He has not seen any case of pernicious anemia following partial gastrectomy. He describes his technic in detail. He also calls attention to several important facts concerning ulcer. First, ulcer of the stomach and duodenum is a local disease dependent on a specific gastritis, free hydrochloric acid in the stomach

contents, and a secondary infection. Second, a radical cure must eliminate all of these factors. Third, experience has shown that partial gastrectomy, because it eliminates all these factors, is most likely to effect a radical cure. The number of recurrences after partial gastrectomy is exceedingly small—about 1 per cent. Investigation has shown that the medical treatment of ulcer is attended by just as grave risks as is surgical treatment, and, unless instituted early, is not likely to bring about radical cure; and that when a patient has had one or two good medical treatments and has not been cured, operative procedure should be undertaken.

End-Results in Cholecystectomy.—Of 352 cases accounted for by Sanders, 269 were completely relieved of the symptoms for which the operations were performed. Forty-two patients reported only partial relief but were improved. Only fourteen were not benefited. The digestion was greatly improved in 306 cases. Only partial relief was obtained in thirty-three cases. Thirteen of the entire group were not relieved or were made worse. The condition of the wound was satisfactory in 91.5 per cent of the cases, whereas a bulge or hernia occurred in thirty (8.5 per cent) of the entire group. The incidence of postoperative hernia was far greater in cases in which the wounds were drained than in cases in which they were not drained. Practically all the hernias that occurred were in the cases in which operation had been done through an upper right rectus incision with the rectus muscle retracted to the outer side. After the operation, 87.2 per cent of the patients did not have colic, whereas 12.5 per cent reported having had one or more spells of "bilious" colic. The pain was similar to the former spells and in practically all cases the patients were afraid of the return of the original trouble. After the colic had subsided there was no jaundice in most cases and the progress was then as smooth as it was in the uncomplicated cases. In two cases, stones were later found in the common bile duct and a secondary operation was necessary. In the remaining number it was not possible to determine the cause of recurrent pain in the absence of any apparent unremoved lesion. Sixteen patients (4.5 per cent) reported the appearance of postoperative jaundice of some degree. This could be accounted for in two cases by the finding of stones in the common bile duct, but in the others the cause was less certain. The icterus soon disappeared and did not leave any bad after-effect.

Surgical Treatment of Urinary Incontinence in Women.—Smith states that a careful plastic repair of the anterior vaginal wall with such other gynecologic procedures as may be indicated will correct the impaired bladder control of which many of these sufferers complain in the majority of instances. When the incontinence is more pronounced, the Kelly operation of tightening the vesical sphincter combined with colporrhaphy gives a cure in a considerable proportion of women with relaxed vesical sphincter. When this procedure failed in a case of severe incontinence, the addition of bladder drainage to the plastic procedure on the sphincteric region supplemented by an interposition gave an excellent result.

Noneffect of Viosterol in Treatment of Fractures.—In seventeen cases of various fractures in adults, most of them fractures of the shafts of the long bones, Lewis studied the effect of viosterol on healing. There was no hastening of union or callus formation. The calcium and inorganic phosphorus in the blood was not materially raised. An average rise of only 1.4 mg. of calcium was obtained and the phosphorus showed relatively no change. Delayed union was present in six cases and no benefit was obtained by using viosterol.

Malignant Tumors and Their Metastases.—A summary of the necropsies in 865 cases of malignant tumor is presented by McWhorter and Cloud. Ninety-five of these were cases of sarcoma, none of which showed any metastases. Among the 770 cases of carcinoma, 187 showed metastases. They were present most often in cases of carcinoma of the esophagus, stomach, large intestine, bladder and liver, the two last named having the highest number (29.17 and 39.19, respectively); only thirty-two of 208 stomach cases showed metastases. No metastases were found in the small intestine, ovary, testicle, thymus, melanoma and tooth bud cases, a total of twenty-three cases. The average age for all malignant tumors at necropsy was 51. Excepting in the very aged, age does not seem to influence metastases. In the aged, the neoplasm was usually of local growth. About 69 per cent of the malignant epithelial tumors arising in, or from, the skin and mucous membrane remained local in their growth, invading either the neighboring lymph glands and adjacent tissues or both, while only 28 per cent of the cases arising in glandular organs showed the same local tendency of growth. One of the interesting observations in this review was the number of cases that showed only local invasion of the neighboring tissues and adjacent lymph nodes. Perhaps of even greater interest are the cases in which the neighboring nodes were alone involved. This held true for carcinomas regardless of their site of origin, but were much more frequently found in the cases whose site of origin was the stomach, large intestine, urinary bladder and cervix. The most interesting feature of this series is the number of cases of supposedly malignant tumors that did not metastasize. Out of 770 morphologically malignant epithelial neoplasms, 187 showed no obvious evidence of metastases. It is suggested that virulence and body resistance may be the guiding factors in the growth of all malignant neoplasms, as they seem to be in all infections.

Archives of Neurology & Psychiatry, Chicago

24: 439-666 (Sept.) 1930

Ganglioglioma: Tumor of Central Nervous System: Two Cases. C. B. Courville, Loma Linda, Calif.—p. 439.
Reaction of Central Nervous System to Experimental Urea Intoxication. B. J. Alpers, Philadelphia.—p. 492.
Changes of Spinal Cord in Hodgkin's Disease: Two Cases with Unusual Skin Manifestation in One. P. F. Shapiro, Chicago.—p. 509.
Blood Electrolyte Changes in Narcosis: Calcium and Potassium. S. Katzenelbogen, Baltimore.—p. 525.
*Incidence of Fever and Leukocytosis in Multiple Sclerosis. J. B. McKenna, Boston.—p. 542.
*Galactose Tolerance in Dementia Praecox. F. H. Sleeper, Worcester, Mass., and R. G. Hoskins, Boston.—p. 550.
Argyll Robertson Phenomenon. W. G. Spiller, Philadelphia.—p. 566.
Vocal Myasthenia of Postencephalitic Origin: Case. D. M. Olkon, Chicago.—p. 570.
Epidemic Encephalitis. H. A. Riley, New York.—p. 574.
Progress in Psychiatry: IV. Experimental Type Psychology. F. Wertham, Baltimore.—p. 605.

Incidence of Fever and Leukocytosis in Multiple Sclerosis.—The study of 109 records of reasonably certain cases of multiple sclerosis is reported by McKenna with reference to the reactive changes in temperature, leukocyte count and examination of the cerebrospinal fluid. Neither fever nor leukocytosis was shown by 40.4 per cent, but three showed increased cell counts in the cerebrospinal fluid. Elevations in temperature were shown by 55.9 per cent, 44.9 per cent between 99 and 99.5 F. and 11 per cent between 99.6 and 100 F. Definite leukocytosis was shown by 22.9 per cent, 3.6 per cent occurring without elevation in temperature and 19.3 per cent accompanying febrile reactions. Pleocytosis of the cerebrospinal fluid occurred in nineteen cases, or 17.4 per cent; three of these cases showed normal temperatures and leukocyte counts; seven were accompanied by fever alone; two by leukocytosis alone, and seven by both fever and leukocytosis.

Galactose Tolerance in Dementia Praecox.—The galactose tolerance was determined by Sleeper and Hoskins one or more times in 135 cases of dementia praecox. The tolerance level was constant in 15 and variable in 24 of the 39 cases in which multiple determinations were made. Similar variability has been noted by others in the blood sugar curves following the ingestion of dextrose. In the series as a whole there was a downward trend of the galactose tolerance, averaging approximately 15 per cent. In 8 per cent of the subjects the tolerance was above normal, and in 58 per cent it was below normal. The catatonic group showed the highest incidence of normal tolerance and the lowest incidence of depressed tolerance. The hebephrenic group showed the lowest incidence of normal tolerance and the highest incidence of lowered tolerance. The galactose tolerance test appears to have some value in the differential diagnosis of the two types. No relationship between weight, age, creatinine output, protein catabolism or initial blood sugar level and galactose tolerance could be detected. There was some evidence of a decrease of tolerance with the increase of the period of hospitalization. A tendency to lowered tolerance for galactose is added to the list of characteristics of dementia praecox that indicate a depression of functions under endocrine or autonomic control.

Archives of Otolaryngology, Chicago

12: 133-272 (Aug.) 1930

Common Cold. A. Hilding, Duluth, Minn.—p. 133.
Embryonic Tissue in Middle Ear and Mastoid: Two Cases. S. J. Crowe and L. M. Polvogt, Baltimore.—p. 151.
*Pneumobacillus (Friedländer's) Meningitis Secondary to Otitis Media: Two Cases. S. Malis, Los Angeles.—p. 162.
Phlegmon of Neck and Osteomyelitis of Mandible Following Tonsillectomy. J. J. Hochfilzer, St. Paul.—p. 175.
Transposition of Section from Auricle for Correction of Nasal Defect: Case. W. W. Carter, New York.—p. 178.
Primary Blastomycosis of Tongue. J. H. Childrey and G. B. New, Rochester, Minn.—p. 184.
Statistical Studies of Children in Public Schools for Deaf. G. E. Shambaugh, D. B. Hayden, E. W. Hagens and R. W. Watkins, Chicago.—p. 190.
Rare Case of Angioma of Ear-Drum, Auditory Canal, Face, Mouth, Tongue, Pharynx and Larynx. H. P. Schugt, New York.—p. 246.
Infection Involving Pharyngomaxillary Space: Two Cases. J. W. White, Norfolk, Va.—p. 248.

Pneumobacillus Meningitis Secondary to Otitis Media.—Malis points out that, clinically and pathologically, septic leptomeningitis due to the pneumobacillus resembles in every way the fulminating type due to the pneumococcus; while cases due to the latter end fatally, those due to the pneumobacillus, if checked early, may be cured. It is therefore of importance to differentiate these two organisms.

Archives of Surgery, Chicago

21: 365-554 (Sept.) 1930

*Adenoid Cystic Carcinoma: Generalized Metastases in Three Cases of Basal Cell Type. J. W. Spies, New Haven, Conn.—p. 365.
*Topographic Relationship Between Nerve Plexuses and Lymph Nodes of Abdomen. F. Kiss, Szeged, Hungary.—p. 405.
Etiology of Neoplasms of Breast: Relation to Other Tumors of Reproductive System. H. C. Taylor, Jr., New York.—p. 412. (C'td.)
*Osteogenic Sarcoma of Humerus: Case. C. B. Morton, University, Va.—p. 444.
*Ureterocele. W. A. Dawley, Rochester, Minn.—p. 458.
*Changes in Head of Femur After Complete Intracapsular Fracture of Neck: Bearing on Nonunion and Treatment. J. V. Santos, Chicago.—p. 470.
Comparison Between Simultaneous Equal-Sized Closed Obstructions of Duodenum and Ileum. J. J. Morton and W. C. Sullivan, Rochester, N. Y.—p. 531.

Adenoid Cystic Carcinoma.—Although there are well authenticated but rare cases in the literature in which ordinary basal cell carcinomas have extended to the regional lymph nodes, Spies failed to find instances in which there were any proved distant or generalized metastases. That such widespread dissemination may occur is believed to be reported here for the first time. Three cases are cited. It is this feature that Spies particularly wishes to emphasize.

Relationship Between Nerve Plexuses and Lymph Nodes of Abdomen.—Kiss asserts that the abdominal lymph nodes lie in close topographic connection with the ganglions and nerve plexuses. Pathologic changes in the lymph nodes, such as hyperemia and enlargement, may cause various nervous symptoms, such as irritation and paresis. The ordinary operative removal of diseased lymph nodes may result in various injuries to the nerves and ganglions. This explains various postoperative complications after such operative procedures.

Osteogenic Sarcoma of Humerus.—The history of a case of telangiectatic osteogenic sarcoma of the humerus is presented by Morton and the recent literature on osteogenic sarcoma briefly reviewed. The principal features of the case were the extreme rapidity of growth of the tumor and the immense size attained by it. Only four months elapsed between the time of the onset of the first symptoms and the death of the patient. The case is discussed briefly from the standpoint of the pathology, diagnosis and treatment.

Ureterocele.—Two cases are reported by Dawley. In neither of these cases was a positive diagnosis made by cystoscopy. Although ureterocele was considered in each, neither presented the usual appearance of ureterocele at cystoscopic examination; the intermittent ballooning and translucence were absent. The etiology is not clear in either case. In one case, the condition was associated with a congenital anomaly of the urinary tract. In both cases, in all probability, the condition had been present for a longer time than the duration of severe symptoms, which in the first case evidently were due to superimposed infection and in the second to obstruction at both ureteral and urethral orifices. Pyuria had been a persistent symptom in both cases. The radical method of treatment was deemed advisable in view of the infected functionless kidneys and the associated pathologic changes in the ureters. In one case, the ureterocele sac was resected transvesically; in the other it was not disturbed.

Changes in Head of Femur After Complete Intracapsular Fracture of Neck.—Fourteen cases form the basis of Santos' study. He says: After complete intracapsular fracture of the neck of the femur, the proximal fragment may either remain alive as a result of nourishment received through the vessels of the ligamentum teres or become necrotic. If efficient reduction and fixation are carried out early and sufficiently long maintained, bony union follows in a high percentage of the cases in which the head remains alive and in a smaller but no inconsiderable percentage of cases in which the head becomes necrotic. If bony union occurs in the presence of necrosis of the proximal fragment, the limb should be protected from weight bearing for many months while creeping substitution of dead head by new bone is taking place. If marked collapse and deformity of the necrotic head should develop, a Whitman reconstruction operation with excision of the head may sometimes be indicated. If nonunion results and the head remains alive, a patient who is a good risk may be operated on by use of an autogenous bone peg or by the Whitman or the Brackett reconstruction method according to the case. In case of nonunion with necrosis of the head, there may be slow invasion of tissue from the round ligament or from adhesions with gradual absorption and partial replacement of the necrotic tissue by living bony elements. However, the proper operative treatment in case of nonunion with necrosis of the proximal fragment appears to be excision of the head and the performance of a Whitman reconstruction operation. By roentgenographic studies, it is usually possible to differentiate between a head that remains alive and one that becomes necrotic because of the difference in density which develops during the period of disuse and because of the difference in internal structure and occasionally in contour which develops during the period of reconstruction.

Arkansas Medical Society Journal, Little Rock

27: 75-91 (Sept.) 1930

Treatment of Bone Infections by Method of Leopold Ollier. A. DeGroat, Fayetteville.—p. 75.
General Practitioner and Diagnosis of Early Tuberculosis. J. D. Riley, State Sanatorium.—p. 77.
Facts Concerning Care of New-Born Child. G. D. Murphy, El Dorado.—p. 84.

Illinois Medical Journal, Oak Park

48: 157-232 (Sept.) 1930

Health Department and Practicing Physician. H. M. Camp, Monmouth.—p. 175.
Uroselectan in Intravenous Urography. J. Welfeld and D. H. Pardoll, Chicago.—p. 179.
Probation: First Line of Defense. G. T. Palmer, Springfield.—p. 187.
Endocrines in Gynecology: Dysmenorrhea and Other Menstrual Disorders. A. G. Gabrielianz, Chicago.—p. 193.
Differential Diagnosis of Pain of Angina Pectoris and Radicular Syndrome of Hypertrophic Osteoarthritis of Spine. D. C. Sutton, Evanston.—p. 202.
Management of Debilitated Surgical Patients. R. K. Packard, Chicago.—p. 206.
County Medical Society and Practicing Physician. L. O. Frech, Decatur.—p. 210.
Tularemia: Case in Chicago. H. G. Leon, Chicago.—p. 214.
Symposium of Mentality. G. G. Kilgour, Chicago.—p. 215.
Treatment of Injuries of Eye. E. F. Garraghan, Chicago.—p. 217.
Preoperative Management of Prostatic. D. F. Rudnick, Chicago.—p. 219.
Arthritis from Medical Viewpoint. S. Fahlstrom, Chicago.—p. 221.
Acute Abdominal Pain. F. G. Dyas, Chicago.—p. 226.

Indiana State M. Assn. Journal, Fort Wayne

23: 395-472 (Sept. 15) 1930

Bilateral Renal Lithiasis. H. G. Hamer, Indianapolis.—p. 395.
New Things in Bacteriology. T. B. Rice, Indianapolis.—p. 401.
Emergency Surgical Operations in Presence of Hyperthyroidism; Acute Hyperthyroidism as Postoperative Complication. J. K. Berman, Indianapolis.—p. 407.
Next Important Step in Administrative Public Health in Indiana. W. F. King, Indianapolis.—p. 411.
Present Status Regarding Etiology of Gastric Ulcer. R. W. Elston, Fort Wayne.—p. 413.
Diphtheria: Pathology. F. Forry, Indianapolis.—p. 416.

Iowa State Medical Society Journal, Des Moines

20: 395-446 (Sept.) 1930

Converging Trend of Medicine and Surgery. E. M. Myers, Boone.—p. 395.
Phases of Cancer Problem. W. R. Jepson, Sioux City.—p. 398.
Diagnosis and Treatment of Early Cancer of Breast. W. L. Hearst, Cedar Falls.—p. 400.
Indications for Treatment in Abortions. H. C. Hesseltine, Iowa City.—p. 406.
Public Health Survey of Iowa. A. J. McLaughlin, Chicago.—p. 409.
Complications of Duodenal Ulcer. G. N. Best, Council Bluffs.—p. 416.
Differential Diagnosis of Pulmonary Tuberculosis, Lung Abscess and Bronchiectasis. F. P. McNamara, Dubuque.—p. 421.
Effect of Complemental Feedings on Initial Weight Loss of New-Born. J. H. Randall, Iowa City.—p. 425.
Indications for Certain Special Diagnostic Blood Studies. J. J. Clemmer, Iowa City.—p. 427.

Johns Hopkins Hospital Bulletin, Baltimore

47: 123-187 (Sept.) 1930

*Prognosis for Epidemic Encephalitis in Children. H. A. Howe, Baltimore.—p. 123.
*Placenta from Case of Malaria. G. B. Wislocki, Baltimore.—p. 157.
Views of Adam Smith on Medical Education. M. S. Guttmacher, Baltimore.—p. 164.
Manner of Anastomosis of Hepatic and Portal Circulations. J. M. Olds and E. S. Stafford, Baltimore.—p. 176.

Prognosis for Epidemic Encephalitis in Children.—A series of sixty-six children was investigated by Howe at periods varying from one to ten years after the onset of epidemic encephalitis. Immediate mortality based on all hospital admissions since 1918 was found to be 11 per cent. Complete incapacity was found in 19 per cent, partial incapacity in 22 per cent, and recovery in 42 per cent. The acute illnesses were divided into three groups: 1. Somatic (56 per cent of the cases), characterized by paralyses or excitation of the somatic or cranial nerves. 2. Meningeal (16 per cent), in which signs of meningeal irritation predominated. 3. Abortive (19 per cent), in which no true acute illness of ordinary encephalitic type occurred but the early and frequently unheralded appearance of characteristic progressive sequelae took place, often accompanied by febrile reaction. The immediate mortality was higher in the somatic group and at early ages; recovery was almost invariable in the meningitic form, and the most dreaded sequel, parkinsonism, ensued most frequently after the abortive form. Sequelae were divided into progressive and nonprogressive, the former including hyperactivity (usually of a bizarre type), sleep inversion, personality changes, hyperpnea and tics, (all excitation phenomena), the latter characterized by residuums of the acute illness in the form of paralyses, choreiform movements, emotional instability and mental retardation. The nonprogressive sequelae most frequently followed the general somatic type of acute illness and, with the exception of mental retardation, offered a good prognosis. Progressive sequelae justified an unfavorable outlook and, when present as initial symptoms, concomitant with the acute illness, almost invariably led to parkinsonism. Parkinsonism was further shown to ensue only after a characteristic type of progressive (excitation) sequelae.

Placenta from Case of Malaria.—The study made by Wislocki of the placenta from a case of malaria affords proof that the chorionic syncytium is incapable of phagocytizing an inert suspension of pigment present in the intervillous spaces or of transmitting such particles from mother to fetus. Malarial parasites are present in the placenta in great abundance within the erythrocytes in the intervillous spaces. Malaria induces the accumulation of large numbers of monocytes and lymphocytes in the placental circulation. Of these cells, the monocytes phagocytize, abundantly, pigment released by the activity of the malarial organisms. These phagocytic monocytes do not penetrate the fetal tissues but do enter the masses of fibrin formed on the villi, which are denuded of syncytium at these sites. Typical clasmatocytes are not encountered in the intervillous spaces. The monocytes and lymphocytes which gather in the placenta are brought there from other parts of the maternal body where they are produced. The villi, including their stroma and covering chorionic syncytium, are anatomically normal and not visibly affected by the malarial organisms or their products. Wislocki suggests that it is unlikely that malarial organisms can enter or penetrate the chorionic syncytium, so that the transmission of malaria from mother to fetus occurs rarely, if at all.

Journal of Immunology, Baltimore

19: 255-340 (Sept.) 1930

Nature of Thermoprecipitins. D. D. Nai, Milan, Italy.—p. 255.
Isohemagglutination: IV. Chances of Proving Nonpaternity; Blood Groups. A. S. Wiener, M. Lederer and S. H. Polayes, New York.—p. 259.
Colloidal Gold Test in Experimental Poliomyelitis. C. W. Jungeblut and D. Khorazo, New York.—p. 283.
Preparation of Antigens from Cultures of Treponema Pallidum. A. B. Wadsworth, J. E. Van Amstel and M. W. Brigham, New York.—p. 289.
Relationship Between Complement and Opsonin: Experiments with Congo Red. J. Gordon, Leeds, England.—p. 303.
Determination of Amounts of Antitoxic Globulin Solution Effective in Sensitizing Guinea-Pig: Amount of Cross Sensitization Between Antitoxic Globulin or Serum Obtained from Horse, Goat and Calf. D. M. Behner, New York.—p. 307.
Typhoid Agglutinin Production: Rôle Dosage, Total Amount of Agglutinogen Injected and Frequency of Inoculation Play. C. A. Behrens and C. H. Keipper, Lafayette, Ind.—p. 321.

Journal of Urology, Baltimore

24: 217-342 (Sept.) 1930

Cystitis Emphysematosa: III. Additional Case in Man, Associated with Cystitis Cystica. R. G. Mills, Fond du Lac, Wis.—p. 217.
*Ascending Infection of Kidney and Kidney Pelvis. C. M. Gruber and J. Rabinovitch, St. Louis.—p. 233.
*Conservative Surgery of Bilateral Hydronephrosis. A. J. Scholl, Los Angeles.—p. 251.
Effect of Denervation of Lower Ureter on Incidence of Ureteral Reflux in Dog. E. H. Barksdale and W. W. Baker, Nashville, Tenn.—p. 263.
Ureteral Stricture: Ureter Above Point of Partial Obstruction. V. Vermooten and B. C. Wheeler, Boston.—p. 269.
*Spinal Anesthesia. M. F. Campbell, New York.—p. 279.
Leiomyosarcoma of Urinary Bladder. H. D. Caylor and W. Walters, Rochester, Minn.—p. 303.
Treatment of Bladder Neck Contracture or Median Bar. H. W. Martin, Los Angeles.—p. 313.
Recurrent Prostatic Hypertrophy: Case. B. Lewis and G. Carroll, St. Louis.—p. 319.
Revolver Bullet Entering Suprapubically and Lodging in Posterior Urethra. M. H. Wyman, Columbia, S. C.—p. 325.
Pioneer Urologist. A. E. MacKay, Portland, Ore.—p. 329.
Intradermal Injections of Gonococcal Bouillon Filtrated. B. C. Corbus and V. J. O'Conor, Chicago.—p. 333.

Ascending Infection of Kidney and Kidney Pelvis.—Gruber and Rabinovitch present experimental evidence which favors the theory that ascending ureteral infections are a cause of pyelitis.

Conservative Surgery of Bilateral Hydronephrosis.—A patient with bilateral hydronephrosis, a large part of the left kidney being completely destroyed and the right kidney less extensively, was treated by Scholl by repeated pelvic lavages followed by freeing of the kidneys from extensive adhesions, partial decapsulation and nephropexy. Two months elapsed between the operations on the two kidneys. The result of this conservative procedure has been highly satisfactory.

Spinal Anesthesia.—Campbell regards spinal anesthesia as being the ideal anesthetic for operations below the diaphragm and of invaluable usefulness in patients suffering from advanced nephropathy. Since the introduction of ephedrine, hypotension is now only a relative contraindication to the application of spinal anesthesia. As with all anesthetics, there are a few rather definite contraindications; the more robust the patient, the less is the anesthetic risk. Untoward immediate postanesthetic sequelae result from temporary bulbar anemia; later post anesthesia sequelae are negligible. In Campbell's series, the ultimate postoperative mortality was 4.4 per cent less in those patients operated on under spinal anesthesia than in those to whom general anesthesia was administered. Of particular interest has been the reduction of the operative mortality following upper urinary tract surgery and prostatectomy.

Kansas Medical Society Journal, Topeka

31: 311-350 (Sept.) 1930

Problems of Cancer. J. C. Bloodgood, Baltimore.—p. 311.
Gastric and Duodenal Ulcers. L. O. Nordstrom, Salina.—p. 316.
Stasis of Cecum and Ascending Colon. L. D. Johnson, Chanute.—p. 322.
Life Conservation. J. W. Graybill, Newton.—p. 327.
Rat Bite Fever. F. Foncannon, Emporia.—p. 331.
Control of Bleeding in Tonsillectomy, Operative and Postoperative. E. M. Freund, Albany, N. Y.—p. 675.
Stammering. R. M. Lukens and M. Trumper, Philadelphia.—p. 680.
Loaded Revolver Cartridge in Bronchus: Case. M. P. Stiles, Birmingham, Ala.—p. 683.
Peptic Ulcer of Esophagus. F. S. Mainzer, Clearfield, Pa.—p. 685.

Medical Journal and Record, New York

132: 209-260 (Sept. 3) 1930

*Infectious Origin of Pernicious Anemia and Relation of Pyelitis to Achlorhydria and Pernicious Anemia. J. Blair, Cleveland.—p. 209.
Brain Tumor (Spongioblastoma) Simulating Encephalitis Involving Frontal Lobe, Basal Ganglia and Third Ventricle. W. C. Menninger, Topeka, Kan.—p. 213.
Vaccines: Use in Control and Cure of Disease. R. O. Clock, Pearl River, N. Y.—p. 218.
Putrefactive Intestinal Toxemia. W. E. Fitch, Bedford, Pa.—p. 221.
Correlation Between Intelligence and Physical Condition in 14,176 Retarded School Children. N. A. Dayton, Boston.—p. 222.
Respiratory Infections in Children. N. Ginsberg, Long Beach, N. Y.—p. 225.
Technic of Spinal Anesthesia with Spinocaine. T. E. Jones, Cleveland.—p. 226.
*Diet in Gallbladder Diseases. M. Einhorn, New York.—p. 227.
*Acute Yellow Atrophy Associated with Neoarsphenamine Injections. A. Bortin, New York.—p. 228.
Gallbladder Disease. H. A. Royster, Raleigh, N. C.—p. 232.
Pathologic Conditions of Liver: Electric Diagnosis and Treatment. J. J. E. Maher, New York.—p. 237.
Toxic Hepatitis Due to Cincophen-Containing Patent Medicine. M. Grolnick, New York.—p. 240.
Recent Advances in Treatment. H. I. Goldstein, Camden, N. J.—p. 243.
California Medicine. J. W. Shuman, Los Angeles.—p. 246.

Infectious Origin of Pernicious Anemia; Relation of Pyelitis to Achlorhydria and Pernicious Anemia.—Blair concludes his review by stating: It seems evident that the actual anemia of pernicious anemia is not due to erythrocyte hemolysis or excessive destruction in the vascular system but is the result of a deficiency in the formation of erythrocytes and that the deficiency is due to a lack of sufficient stroma material required for the formation of the erythrocytes. In pyelitis there is a constant loss of granular leukocytes from the body and the occurrence of pyelitis in pernicious anemia constitutes an insistent demand for granular leukopoiesis. There are certain common relationships between erythrocytes and granular leukocytes: (*a*) They are formed in the same location, in bone marrow, in the adult; (*b*) both erythrocytes formation and granular leukocyte formation are decreased in the relapse of pernicious anemia; (*c*) they exhibit a simultaneous response to liver therapy. It seems probable that the excessive production of leukocytes over a long period exhausts from the body the substance (the specific x factor of liver) necessary to both granular leukocyte and erythrocyte formation and is thus responsible for the anemia and leukopenia. It seems probable that the achlorhydria present in pernicious anemia is the end-result of a chronic mild stimulation of gastric secretion associated with a mild chronic infection (pyelitis, and producing an exhaustion of the secreting mechanism of the stomach from overuse, coupled with an exhaustion from the stomach tissues themselves of the specific x factor present in normal stomach tissues. It would seem that the presence of pyelitis in pernicious anemia gives adequate explanation for the presence of fever, loss of weight, the tendency to remission and relapse, and other symptoms. The prevention of pernicious anemia is therefore the prevention of focal infection and consequent urinary tract infection, the detection and cure of focal infection and urinary tract infection already established, and the preventive or palliative administration of the specific substance found abundantly in liver.

Diet in Gallbladder Diseases.—The following rules are laid down by Einhorn for all gallbladder patients. 1. Meals should be ingested frequently (at not too long intervals), in order to induce a complete emptying of the gallbladder quite often. 2. Each meal should consist of mixtures containing the three principal groups of nutritive materials (proteins, carbohydrates, fats) in the right proportions. Excesses in the quantity of food, also too luxurious meals, should be carefully avoided. Likewise too much spice, too much meat, too much beer or wine are to be guarded against. Attention should be given to procuring daily a thorough evacuation of the bowels. Outdoor sports should be indulged in, and long walks—but not to a degree of overfatigue—should be practiced. Increase of the intake fluids should be encouraged. In gallbladder cases, without jaundice, practically all kinds of ordinary foods, excepting highly indigestible or strongly spiced substances, are permissible. In gallbladder diseases, with jaundice, special attention must be paid with regard to the selection of an appropriate diet. Fats are poorly utilized and should therefore be used with great moderation. The following may be arranged as a daily quantum of foods: 2½ quarts of skimmed milk, 870 calories; 100 Gm. of wheaten bread, 245 calories; 100 Gm. of oatmeal (flour), 338 calories, and 100 Gm. of sugar, 400 calories, to which can be added some fresh fruit and a green vegetable. A little later one or two eggs are added. In order to increase the digestibility of the nutritive material pancreatic ferments are advantageously administered. It is then feasible to make the bill of fare more varied, with much profit to the patient. Malignant diseases of the gallbladder and biliary ducts will have to be treated dietetically in a similar manner as the benign disorders of these organs. At first the diet as outlined will be employed. When, however, the disease has already made greater inroads and the usual foods cannot be handled by the patient, the diet will have to be selected mostly from liquid and semisolid nutriments. Milk, buttermilk, koumiss, gruels, broths, eggnogs, sweet almond milk, fruit juices, and jellies will play a great part. An attempt must always be made to keep the organism from losing too much, but toward the end it is seldom possible to supply adequate nutrition. Everything in the line of feeding must be selected in such a manner that it will give comfort and pleasure to the patient until life is ended.

Acute Yellow Atrophy Associated with Neoarsphenamine Injections.—A case is reported by Bortin of a patient with tertiary syphilis who during a course of mercury and neoarsphenamine developed jaundice and died, with changes in the liver not unlike those of acute yellow atrophy. The probable immediate cause was the injection of neoarsphenamine. The predisposing cause of acute yellow atrophy was the injections of mercury.

New England Journal of Medicine, Boston

203: 499-548 (Sept. 11) 1930

Obstetric Aspect of Intracranial Hemorrhage. F. C. Irving, Boston.—p. 499.
*Symptomatology and Immediate Treatment of Cranial and Intracranial Injury in New-Born, Including Intracranial Hemorrhage. D. Munro, Boston.—p. 502.
*Late Effects of Obstetric Injuries at Various Levels of Nervous System. R. K. Byers, Boston.—p. 507.
*Significance of Acidophilic Cells in Thyroid Gland. S. Warren and W. Stoller, Boston.—p. 523.
Future of Tuberculosis Control. K. Emerson, New York.—p. 524.
Summary of What Has Been done at Lakeville. Z. B. Adams, Boston.—p. 526.
Value of Such Institution as Lakeville to Practitioner. E. O. Otis, Exeter, N. H.—p. 527.
Considerations with Respect to Nonpulmonary Tuberculosis. W. P. Bowers, Boston.—p. 529.
Services Available at Lakeville State Sanatorium, Middleboro, Mass. L. A. Alley, Middleboro, Mass.—p. 531.

Immediate Treatment of Intracranial Injury in New-Born.—A detailed consideration of the symptoms observed in 117 cases of cranial and intracranial injury in the new-born, together with a brief consideration of the immediate treatment of these conditions, is presented by Munro. A first baby that is hypertonic, apathetic, refuses to nurse and has a tense anterior fontanel, an abnormal cry and some respiratory abnormality is presumably suffering from some form of intracranial injury. If the cerebrospinal fluid pressure is higher than normal, this diagnosis is confirmed. A first baby that is pale and flaccid, refuses to nurse and has a respiratory abnormality immediately after delivery is presumably suffering from surgical shock. If the cerebrospinal fluid pressure is less than normal, this diagnosis is confirmed. In the presence of surgical shock, treatment should be reduced to the absolute minimum. In the presence of hemorrhagic disease of the new-born, complicating cranial and intracranial injury, the bleeding and clotting times should be brought to normal before decompressive treatment is begun. All types of cranial and intracranial injury in the new-born are complicated at some time by an increased intracranial pressure. Treatment of this complication never should be omitted. The diagnosis "intracranial hemorrhage of the new-born" should be expanded to include cerebral edema and fracture of the skull and should be stated as "cranial and intracranial injury in the new-born."

Effects of Obstetric Injuries on Nervous System.—The possible effect of obstetric trauma to the nervous system

of the new-born is discussed by Byers. Case histories are briefly given illustrating the results of lesions involving the nervous system from peripheral nerves to cerebral hemispheres. Attention is called to a method of treatment that is effective provided there exists an intact nervous pathway from a functionally active cerebral cortex to the muscles.

Significance of Acidophilic Cells in Thyroid Gland.—Warren and Stoller present a summary of the cases in which excised thyroid tissue showed acidophilic cells. From 1923 to 1929 this change was encountered in seventy-five patients, thirteen of whom developed actual or suspected postoperative myxedema. Since less than 20 per cent of patients whose thyroids showed acidophilic cells became myxedematous, the presence of these cells is not of practical prognostic value, although it is perhaps a more definite sign than any other.

203: 549-612 (Sept. 18) 1930

*Treatment of Carbuncles by Roentgen Ray: Analysis of Fifty Cases. R. U. Light and M. C. Sosman, Boston.—p. 549.
Physiologic Basis of Surgery of Sympathetic Nervous System. J. F. Fulton, New Haven, Conn.—p. 555.
Analysis of Cases of Infantile Paralysis Treated at Shriner's Hospital for Crippled Children, Springfield, Mass., During 1925. R. N. Hatt and G. deN. Hough, Jr., Springfield, Mass.—p. 561.
Progress in Study of Cardiovascular Disease in 1929. E. F. Bland and H. B. Sprague, Boston.—p. 574.

Treatment of Carbuncles by Roentgen Ray.—From a study of fifty cases of carbuncle treated with roentgen ray, Light and Sosman conclude that when benefit occurred it lay usually in a hastened necrosis of the lesion, a softening or liquefaction of a carbuncle in the indurated stage. In a few instances the spreading tendencies of the lesions were checked, and healing occurred by drying up and absorption without any extensive drainage of necrotic products. Roentgen therapy was occasionally employed with success following surgical procedures which failed to halt the spread of the carbuncle, and in these the acidity of the infectious process was diminished and the peripheral spread halted. Relief of pain occurred in some instances of cervical carbuncles and, quite strikingly, in most of those of the face. Of the entire series, thirty-four patients were observed to have been improved by roentgen therapy, and sixteen to have received no benefit from this treatment. Thirteen out of fifteen women patients were improved; three fifths of the men, when the site of predilection was the neck, were helped by irradiation. Eight of the nine carbuncles of the face responded excellently, as did most of those of the extremities. The proportionate success of roentgen therapy diminished somewhat with the increasing size of the lesion; 75 per cent of those under 5 cm. diameter were benefited, whereas but 60 per cent of those larger than 9 cm. diameter improved as a result of roentgen ray. Diabetes seemed to have little bearing on the chances of success from irradiation.

New York State Journal of Medicine, New York

30: 1077-1142 (Sept. 15) 1930

Bronchiectasis: Analysis of Fifty-One Cases. W. W. Priddle, Toronto, Canada.—p. 1077.
*Simple Dietetic System for Use in Metabolic Disorders. I. J. Levy, New York.—p. 1084.
Treatment of Intra-Oral Cancer: Radium Therapy. D. Quick, New York.—p. 1094.
*Home vs. General Hospital Childbirths. W. B. D. Van Auken, Troy.—p. 1096.
Hemopneumothorax of Uncertain Etiology: Case. A. H. Terry, Jr., New York.—p. 1100.
Remedy for Fee-Splitting Among Doctors. G. F. Chandler, Kingston.—p. 1103.
What Orthopedic Conditions the General Practitioner Has to Look for in Periodic Examination. S. W. Boorstein, New York.—p. 1107.

Simple Dietetic System for Use in Metabolic Disorders.—Levy's system is based on a key chart in which similar foods have been grouped so that varying quantities have similar distribution of protein, carbohydrate and fat. From this chart, diets of any caloric value or any desired distribution of foodstuffs may be derived. Specimen diets are given.

Home vs. General Hospital Childbirths.—Home and general hospital childbirths are discussed by Van Auken with reference to proper preparations, obstetric emergencies, infections, nursing services, the physicians' and patients' attitude, and the relative financial cost. It is obvious from this article that, except for the possible greater frequency of infection in the general hospital and the limited ability of the nursing service for patients unable to afford a full time nurse, the general hospital is a more advantageous place for a childbirth. Home childbirths are desirable and successful when there are no complications and when the patient does not want the maximum relief from her pain. As it is impossible always to predict complications, general hospital childbirths insure greater safety.

Rhode Island Medical Journal, Providence

13: 127-144 (Sept.) 1930

Management of Convalescence in Rheumatic Heart Disease. W. P. Buffum, Providence.—p. 127.
Treatment of Neurosyphilis. W. C. Weigner, Providence.—p. 130.
Sinusitis in Infants and Children. N. A. Bolotow, Providence.—p. 134.

Tennessee State Medical Assn. Journal, Nashville

23: 313-352 (Sept.) 1930

Chronic Retrobulbar Neuritis. W. H. Wilmer, Baltimore.—p. 313.
Rationale of Hysterectomy Following Cesarean Section in Cases of Intra-Uterine Infection. J. L. Crook, Jackson.—p. 325.
Puzzling Types of Indigestion. W. C. Alvarez, Rochester, Minn.—p. 330.

Virginia Medical Monthly, Richmond

57: 355-424 (Sept.) 1930

Tardy Symptoms of Congenital Lesions. O. H. P. Pepper, Philadelphia.—p. 355.
Depressor Substance of Liver in Treatment of Hypertension. J. D. Willis, Roanoke.—p. 361.
Symptomatology of Hypothyroidism. P. S. Smith, Abingdon.—p. 365.
Varicose Veins. J. O. Fitzgerald, Jr., Richmond.—p. 368.
Ligation of External Carotid Artery to Control Nasal Hemorrhage. A. T. Hawthorne, Winchester.—p. 370.
Cerebral Thrombosis. M. J. Payne, Staunton.—p. 372.
Injuries of Carpal Bones of Wrist: Case of Dislocation of Semilunar Bone and Fracture of Scaphoid Bone and Ulnar Styloid. R. L. Anderson, Richmond.—p. 381.
Epidural Sacral and Parasacral Anesthesia in Surgery of Perineum. J. W. Sayre, Newport News.—p. 384.
Eugenic Sterilization. E. R. Mickle and C. E. Holderby, Williamsburg.—p. 387.
Venereal Disease Prevalence in Virginia. L. J. Usilton and W. D. Riley, Washington, D. C.—p. 389.
Perineotomy Versus Laceration. R. P. Kelly, Lynchburg.—p. 397.
Optic Neuritis: Tonsil as Etiologic Factor. W. O. Bailey, Leesburg.—p. 401.
Acute Anterior Poliomyelitis. C. F. Graham, Wytheville.—p. 402.
Suppurative Arthritis Due to Hemophilic Bacteria. F. W. Shaw, Richmond.—p. 404.
Tularemia in Virginia—1929. H. G. Grant, Richmond.—p. 406.

West Virginia Medical Journal, Charleston

26: 513-576 (Sept.) 1930

Private Practice and Public Health. G. H. Bigelow, Boston.—p. 513.
Choice of Anesthetic Adaptable to Patient and Disease. C. F. McCuskey, Rochester, Minn., and F. M. Moxon, Milwaukee.—p. 521.
Agranulocytosis: Three Cases. F. C. Hodges, Huntington.—p. 532.
Rectal Narcosis with Avertin. C. C. Greer, Clarksburg.—p. 538.
Importance of Proctoscopic Examination in Early Diagnosis of Carcinoma of Rectum and Sigmoid. W. P. Black, Charleston.—p. 540.
Diagnosis and Management of Lateral Sinus Thrombosis. E. C. Hartman, Parkersburg.—p. 541.
Diverticulitis of Colon: Acute Perforations of Sigmoid. R. W. Whitman, Roanoke, Va.—p. 544.
Pyelitis in Infancy and Childhood. K. M. Jarrell, Beckley.—p. 550.
Sporadic Typhoid Fever with Discovery of Carrier. R. S. Spray, Morgantown.—p. 553.
Acute Ileocolitis (Septic). A. H. Hoge, Bluefield.—p. 554.
Exophthalmic Goiter in Child Aged Six Years. H. Garred, Charleston.—p. 555.
Buried Skin Grafts in Burns of Children. E. B. Henson, Charleston.—p. 557.
Interesting Chest Case. J. W. Moore, Charleston.—p. 559.

Wisconsin Medical Journal, Madison

29: 489-548 (Sept.) 1930

Undulant Fever in Wisconsin. H. M. Guilford, Madison.—p. 489.
Agglutination Reaction in Diagnosis of Undulant Fever. W. D. Stovall and M. Crosswait, Madison.—p. 493.
Uterosalpingography in General Practice. J. M. Johnson, Ripon.—p. 497.
Medical Aspects of Nursery School. B. T. Haessler, Milwaukee.—p. 504.
Principles of Roentgen Therapy: IX. Roentgen Therapy in Dermatology. E. A. Pohle, Madison.—p. 507.
Primary Bilateral Carcinoma of Breasts: Two Cases. R. H. Jackson, J. A. Jackson, G. H. Ewell, Madison.—p. 512.
Echinococcus Cysts of Abdomen and Lung: Case. J. P. Zohlen, Sheboygan.—p. 515.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British J. Actinotherapy & Physiotherapy, London

5: 111-132 (Sept.) 1930

Control of Common Colds by Ultraviolet Rays. G. H. Maughan and D. F. Smiley.—p. 115.
Uses of Static Electricity: Treatment of Enlarged Prostate. R. Creasy. —p. 115.
Remedial Treatment of Scoliosis. A. B. Broman.—p. 118.
Whirlpool Bath Leg Rest. W. Bierman.—p. 120.
Treatment of Erysipelas by Ultraviolet Light. R. K. Brown.—p. 121.
Filters for Use in Actinotherapy. A. Furniss.—p. 123.
Balneotherapy and Dietotherapy in Treatment of Arteriosclerosis. W. E. Fitch.—p. 125.

British J. Experimental Pathology, London

11: 217-286 (Aug.) 1930

Intra-Ocular Pressure and Drainage of Aqueous Humor. F. Ridley. —p. 217.
*Acidity and Chloride Content of Gastric Juice. G. V. Rudd.—p. 240.
*Value of Copper Sulphate Tellurite Medium for Isolation of Diphtheria Bacilli. V. D. Allison.—p. 244.
Use of Heparin-Plasma for Grafting of Spontaneous Mammalian Tumors into Homologous Animals. M. J. A. Des Ligneris.—p. 249.
Relative Amounts of Lysozyme Present in Tissues of Some Mammals. H. Florey.—p. 251.
*Flicker Hemoglobinometer. C. E. Jenkins.—p. 261.
Tar Cancer in Mice: 1. Technic of Comparative Experiment. A. F. Watson and E. Mellanby.—p. 267.
Rous Sarcoma No. 1: Loss of Filtrate Activity at Incubator Temperature: Protection by Means of Hydrocyanic Acid. W. E. Gye and W. J. Purdy.—p. 282.

Acidity and Chloride Content of Gastric Juice.—A comparison of the gastric secretory response to a meal of gruel and to one of cream was made by Rudd. A fractional analysis of the gastric contents was carried out and total and neutral chloride and total acidity were estimated in the samples. The total chloride content of the gastric secretion was found to remain approximately constant, while the total acidity and neutral chloride show wide variations. The theory of the formation of neutral chloride by the neutralization of gastric acid by duodenal fluid does not explain these results. It is concluded that the variations in the composition of the gastric contents are due to changes in the amounts of hydrochloric acid and neutral chloride being secreted by the gastric mucosa. In an estimation of the secretory activity of a stomach, the total chloride is the significant quantity.

Copper Sulphate Tellurite Medium for Isolation of Diphtheria Bacilli.—Allison compared the results obtained in the isolation of *C. diphtheriae, C. hofmannii* and diphtheroid bacilli from nasal, throat and ear swabs, using Douglas' medium and copper sulphate tellurite serum agar. The results show a well marked difference in the percentages of organisms isolated on the two mediums, the differences in all cases being in favor of the copper sulphate medium. The better results obtained with the copper sulphate medium are believed to be due to its greater selective action for the diphtheria bacillus and organisms of the diphtheroid group, and to the powerful inhibitory action of the copper sulphate on staphylococci, streptococci and other commensal organisms found in the nose, throat and ears. Inhibition of the spread of *B. proteus*, resulting from the presence of copper sulphate in the medium, facilitated isolation of *C. diphtheriae*, when this had proved impossible with other mediums.

Flicker Hemoglobinometer.—The instrument devised by Jenkins consists of two fixed lights and a Simmance-Abady photometer head in a fixed position between them. The brightness is varied by the depth of a glass plunger in a cup containing a colored solution through which the light from one of the lamps passes. A glass cell is placed between the head and the other light and contains the sample to be examined. With a capillary pipet, 0.1 cc. of blood is added to 4.9 cc. of distilled water in a small bottle or flask. The solution is gassed, centrifugated, and estimated in the apparatus after first checking the balancing point of the standard at 40 mm. The reading obtained is read on the graph in terms of percentage in Haldane's scale or any other scale which the observer chooses to use. If preferred, an actual blood standard of 2 per cent CO-hemoglobin prepared by the makers of the Haldane apparatus can be used instead of the artificial standard of cobalt chloride.

British Medical Journal, London

2: 309-340 (Aug. 30) 1930

Technic of Radium Therapy Today. D. C. L. Fitzwilliams.—p. 309.
Treatment of Pruritus Ani and Anal Fissure. W. B. Gabriel.—p. 311.
Anesthetic Explosions. K. B. Pinson.—p. 312.
Cerebral Hemorrhage in Young Woman. S. C. Lewsen.—p. 313.
*Old-Standing Tuberculous Kidney: Case. J. J. Conybeare.—p. 314.
Hemorrhagic Dry Bronchiectasis. A. J. S. Pinchin and H. V. Morlock. —p. 315.
Four Different Types of Blood Sugar Curve in One Patient Within Seventeen Months. F. J. G. Lishman.—p. 318.
Subsequent History of Patients Treated with Residual Antigen of B. Tuberculosis. C. E. Jenkins.—p. 318.
Tuberculous Adenitis with Dermal Bullae. R. C. Holderness.—p. 319.
Congenital Umbilical Hernia of Liver and Bowel. K. A. Allison.—p. 319.

Old-Standing Tuberculous Kidney.—Conybeare reports a case of what probably was an instance of spontaneous cure of a tuberculous kidney by its being transformed into an innocuous calcareous mass. The whole of the organ appears to have become replaced by a tuberculous pyonephrosis of enormous dimensions, and the tuberculous caseous material has become so infiltrated with lime salts as to produce a dense shadow to roentgen rays. The ureter of the affected kidney has never been permanently occluded, as evidenced by the shadows in the roentgen film. Inquiries from the patient elicited the fact that from time to time he experienced a sensation "as if a tap had been turned off in the bladder." This was followed by the passage from the urethra of cretaceous material, which the patient described as like tooth-paste in color and consistency. It would appear, therefore, that from time to time some of the caseous material from the kidney was passed in the urine. No tubercle bacilli could be found, and probably the tuberculous process is completely arrested. The acute symptoms with which the patient started a recent illness were presumably due to an exacerbation of his chronic urinary infection preventing satisfactory functioning of his right kidney. The case tends to show that, even when there is high resistance to tuberculous infection, involvement of the kidney may lead to serious consequences as the result of secondary urinary infection; it emphasizes the importance of nephrectomy whenever the condition of the other kidney warrants this step being taken.

Journal of Hygiene, London

30: 267-401 (Aug.) 1930

Systemic Influences in Immunity and Cancer. A. Eastwood.—p. 267.
*Vitamin A Deficiency and Resistance Against Specific Infection. H. C. A. Lassen.—p. 300.
Comparative Biometric Study of Albino and Colored Guinea-Pigs from Point of View of Suitability for Experimental Use. G. W. Dunkin, P. Hartley, E. Lewis-Faning and W. T. Russell.—p. 311.
*Serum Treatment of Scarlatina. M. E. Wylie.—p. 331.
Occurrence, Characteristics and Specificity of Natural Agglutinins. H. J. Gibson.—p. 337.
Beriberi and Other Food-Deficiency Diseases in Newfoundland and Labrador. W. R. Aykroyd.—p. 357.
Acute Bacillary Dysentery in Khartoum Province, Sudan: Bacteriophage Treatment. D. Riding.—p. 387.

Vitamin A Deficiency and Resistance Against Specific Infection.—Experiments made by Lassen showed clearly a pronounced decrease of resistance in rats with symptoms of vitamin A deficiency. Within four days after subcutaneous inoculation with living Breslau bacilli, eight out of nine animals with dietary xerophthalmia died, while eight animals on an adequate diet lived more than thirty-seven days. Necropsy of the control animals reveals that the infection persists in the lymph glands, especially the regional glands, a long time after the general infection has been overcome.

Serum Treatment of Scarlatina.—Wylie reports the results obtained in the treatment of 116 cases of scarlet fever with a commercial concentrated antitoxin. The patients came from all types of homes and represented all grades in the social scale. The medical treatment was essentially the same in all cases. In uncomplicated cases patients were allowed up on the twenty-eighth day and dismissed on the forty-second day from the onset of the illness. Complications of the same type were treated similarly. The only variable factor in the treatment was the administration or nonadministration of antitoxin or convalescent serum. Twenty-nine patients did not receive serum of any kind. Eighty-four patients were treated with the concentrated antitoxin, of whom seventy received 10 cc. of antitoxin and fourteen received from 20 to 30 cc. of antitoxin.

Convalescent serum in doses of from 6.5 to 8 cc. was given in three cases. The most striking result of the administration of the antitoxin in the first few days of illness was the rapid clinical improvement as shown by the disappearance of the toxemic symptoms. Vomiting ceased, the throat became less painful, the cervical glands diminished in size, cyanosis disappeared, the rash faded, and moderate desquamation was followed by fine unobtrusive powdering. With the fading of the rash, usually in from six to twelve hours after the administration of serum, there followed a critical fall of temperature, from hyperpyrexia to a subfebrile level, accompanied by a general improvement in the pulse. The patient emerged from the acute stage of the disease to the security of convalescence. The incidence of complications was greater in mild cases which were not treated with antitoxin than in more severe cases treated with 10 cc. of antitoxin. While there is evidence that scarlet fever streptococcus antitoxin has some definite effect in reducing the occurrence of nonseptic complications, there is no evidence that scarlet fever streptococcus antitoxin (*a*) diminishes the occurrence of septic complications, (*b*) delays the onset either of septic or of nonseptic complications, or (*c*) shortens the duration of septic or nonseptic complications.

Lancet, London

2: 383-434 (Aug. 23) 1930

Diabetes as Physiologic Problem. J. J. R. MacLeod.—p. 383.
*Medical Treatment of Cancer. A. T. Todd.—p. 389.
*Rheumatism in Childhood. W. Sheldon.—p. 394.
Protein Milk in Infant Feeding. N. Hill and A. W. C. Mellor.—p. 398.
Catheter Extraction of Ureteral Stone per Urethram. E. H. R. Altounyan.—p. 399.
Eclampsia Treated with Spinal Anesthesia: Case. R. H. Paramore.—p. 399.

Medical Treatment of Cancer.—Todd and his associates have been using a combination of lead with selenium in the treatment of cancer. The preparation is available to all, being a 0.4 per cent solution of lead selenide, a nontoxic colloid. As much as 33 cc. has been given in one dose without adverse effects. The size of the initial dose depends on the nature of the neoplasm. The colloid is injected intravenously at weekly intervals. The size of the later injections depends on the amount of focal and general reaction. It is claimed that the treatment has a favorable action in the majority of the cases; it is estimated that in about one fifth of the patients there is no appreciable result, but in the remainder more or less improvement is found to follow. Radiation therapy concurrently with selenide is also employed. There have been results which give promise of this combination being useful. In view of the known fact that lead tends to be stored in the bones as a compound lead-calcium phosphate, he considered that the patients ought also to be treated with any substance likely to diminish this storage; otherwise any condition associated with acidosis would occasion a liberation of unknown amounts of ionic lead from the skeleton and cause lead poisoning. The obvious remedy was calcium chloride, which was given to all patients daily. In the hope of increasing the assimilation of calcium, patients are given the fat-soluble vitamins. Large doses of vitamin D appear to be really useful when the amount of oily solvent can be tolerated. A small daily dose of thyroid extract is also given, and finally, to combat the anemia usually present in advanced cancer and the anemia occasioned by prolonged injection of lead compounds, they give the patients liver extract. In conclusion, Todd advises that such cancers be treated as are likely to be influenced with radiation first, and as thoroughly as possible. After irradiation is over and the patient has had time to recover, treatment should be instituted by his method. In inoperable cancer as much as possible should be removed by surgical means and afterward one should attempt to make the remainder regress with selenide. Especially he advises giving the treatment after operations which are regarded as having been complete. Finally, he strongly advises that the whole of the method be used: (1) lead selenide to increase local and general defense mechanisms; (2) calcium chloride to increase ionized calcium by acidosis, to correct alkalosis, and to furnish a depot for calcium assimilation; (3) fat-soluble vitamins in large doses, especially vitamin D, to increase calcium absorption and to combat any infective element; (4) small doses of thyroid extract as a tonic and antiinfective agent; (5) liver extract to combat anemia.

Rheumatism in Childhood.—Sheldon states that unless it can be shown that tonsillectomy has a definite influence in the prevention of cardiac disease, there seems small justification for the operation merely on the ground that the child is a rheumatic subject. Of 600 consecutive cases of rheumatism at the rheumatic clinic at Great Ormond Street, tonsillectomy has been performed in no less than 540 (90 per cent). Of these patients, 393 were operated on before their admission to the clinic. In approximately one third of the cases of rheumatic pains, chorea and rheumatic fever commenced these symptoms of rheumatic infection after the tonsils had been removed. In addition, the pains continued after the operation in half of 105 children who had rheumatic pains in the limbs before the removal of their tonsils; and of 93 children who had chorea before removal of their tonsils the chorea relapsed after the operation in 27 per cent. Analysis of 266 children with rheumatic heart disease showed that in 46 cases (17 per cent) the tonsils had been removed before signs of cardiac disease were discovered. It seems more probable that the value of tonsillectomy in rheumatic children is in proportion to the degree of impairment of the general health attributable to the tonsils. In other words, the tonsils of rheumatic children should not be removed unless there is evidence that they are affecting the general health adversely. Such evidence as a history of repeated sore throat, chronic enlargement of the tonsillar glands in the neck, and the appearance of the tonsils must all be taken into consideration. The size of the tonsils alone is an unreliable guide, small scarred tonsils being often as injurious to the child's health as hypertrophied tonsils.

2: 509-560 (Sept. 6) 1930

Synthetic Activities of Animal Cell. H. S. Raper.—p. 509.
Diabetes as Physiologic Problem. J. J. R. MacLeod.—p. 512.
*Lung Puncture in Acute Lobar Pneumonia. D. Stewart.—p. 520.
*Glandular Fever. J. O. W. Bland.—p. 521.
*Apparatus Designed to Diminish Incidence of Postoperative Thrombosis. L. R. Braithwaite.—p. 524.
*Purpura Simulating Acute Abdomen. I. Fraser.—p. 525.
Triketohydrindenehydrate as Reagent for Albumin, Peptone and Amino-Acids. H. Gardner.—p. 525.

Lung Puncture in Acute Lobar Pneumonia.—In cases of acute lobar pneumonia without sputum, or with very little sputum, where for therapeutic reasons it is desirable to know the type of organism as soon as possible, Stewart advocates lung puncture. Lung puncture was performed in seventeen cases of acute lobar pneumonia. A pneumococcus was isolated from the "lung fluid" in thirteen out of seventeen cases.

Glandular Fever.—One case is cited by Bland in which inoculation of the blood into a rabbit was followed by a disease which is transmissible to other rabbits by the citrated blood. This disease is characterized by fever, anemia, leukopenia and monocytosis, enlargement of the lymph glands, spleen and liver, and the production of focal necroses in them. The relationship of this disease to human glandular fever is discussed. The name "experimental glandular fever" is suggested for the disease in rabbits.

Apparatus Designed to Diminish Incidence of Postoperative Thrombosis.—Braithwaite uses a simple form of gymnastic apparatus. There are three pulleys, one (double) at the head and one each (single) at foot and hand. The apparatus is fixed to the head rail of the bed and is used first on one side and then on the other. A light cord is threaded through the pulleys and there is a means of lengthening or shortening the length of the cord. The stirrup and handle are of soft, well padded canvas. It is used for all abdominal operations, beginning as a rule on the fourth day. Some patients will try it earlier and others cannot and will not use it until later; some will not use it at all. At the beginning the patients can exercise for only about two minutes, but the time soon arrives when they are able to work the apparatus for five minutes at each side. In some cases they enjoy the exercise and will ask for it and work it for longer periods. The idea underlying the exercises is to prevent stagnation of blood, especially in the pelvis and lower part of the abdomen. By pushing with the hand the leg is pulled well up to the abdomen and at the same time good exercise is given to the arm. People who have assiduously carried out these daily "jerks" are not only happier for it while in bed but when the time arrives to get up they are much better able to move about.

Purpura Simulating Acute Abdominal Conditions.—In one of Fraser's cases a diagnosis of intussusception was made. Free fluid was found in the peritoneal cavity, and the intestinal wall and mesentery were studded with petechial hemorrhages and ecchymosed patches. Careful examination later revealed many minute small hemorrhagic points which had escaped notice with artificial light. These pinpoint hemorrhages were more marked during the convalescent period. In the other the diagnosis was acute gangrenous appendicitis. At operation a large quantity of nonpurulent blood-stained fluid escaped. The last two feet of the ileum were brilliant scarlet and showed numerous small black areas of hemorrhage. The intestinal wall was markedly thickened with the blood contained in the tissues. The hemorrhage stopped more or less abruptly at the ileocecal valve, leaving the cecum almost normal. The appendix was normal in every respect except that it contained a rich supply of threadworms. The rest of the ileum was mottled, the mottling gradually decreasing toward the jejunum. There were several enlarged mesenteric glands, some soft and others calcified. An examination of the abdominal viscera through this limited incision failed to reveal any further pathologic change. For three or four days after the operation the motions were mixed with dark blood, and on the third day the urine was heavily tinged with blood. The postanesthetic vomit contained blood and the saline solution returned after operation was tinged. On about the tenth day she had a severe attack of epistaxis, and about the same time a marked purpuric rash appeared, involving both feet and the outer sides of the ankles. This was so severe that the feet were almost blue. There was also considerable swelling of the ankles.

Annales de l'Institut Pasteur, Paris

45: 157-289 (Aug.) 1930

Healing of Necrotic Lesions Produced by Large Inoculations of B C G. J. Zeyland.—p. 157.
Biologic Properties of B C G Strain. M. Tzeknovitzer.—p. 162.
*Bacillus Gangrenae-Cutis. R. Nativelle.—p. 169.
Antagonistic Action of Alexin in Phenomena of Agglutination. V. Anthadse.—p. 203.
Sodium Salt of Acetarsone in Treatment of Human Trypanosomiasis. A. Sicé.—p. 221.
Endoglobular Corpuscles in Blood of Lizards. G. Mirone.—p. 243.
*Zinc Content of Animal Bodies. G. Bertrand and Y. Beauzemont.—p. 247.
Critical Temperature of Serum. P. Lecomte du Noüy.—p. 251.

Bacillus Gangrenae-Cutis.—Nativelle describes *Bacillus gangrenae-cutis,* first studied by Milian, which occurs with great frequency in many primary and secondary disseminated cutaneous gangrenes, in genital gangrenes and in scabs from various sources and in ulcers of the leg. While not usually the sole cause of gangrene, this bacillus is an important secondary germ of infection and often causes simple lesions and ulcers to develop into gangrene. Intravenous injections of arsphenamine counteract the action of the bacillus and have a curative effect on the gangrene itself.

Zinc Content of Animal Bodies: Age Variations: Influence of Milk Diet.—Bertrand and Beauzemont proved through experiments on seventy-one white rats that the proportion of zinc in the bodies of animals decreases from the time of birth to weaning because of the deficiency of zinc in the milk diet. The zinc content then increases throughout the period of rapid growth and remains constant in adults. In old age it again shows an increase.

Annales des Maladies Vénériennes, Paris

25: 561-640 (Aug.) 1930

Antichancroid Bacteriophagia. H. Gougerot, E. Peyre and Basset.—p. 561.
Cultivation of Streptobacilli of Ducrey. A. Basset.—p. 569.
*Test for Presence of Gonococcal Antigen in Urine. N. M. Ovtchinnikov and E. M. Séméniako.—p. 577.

Test for Gonococcal Antigen in Urine.—Ovtchinnikov and Séméniako discuss the value of the test for the presence of gonococcal antigen in urine as determined by the complement fixation reaction developed and used by Lissonsky in testing for tuberculous infection. Observation of several hundred cases shows that this reaction is a valuable auxiliary method of diagnosis, especially in determining the moment of disappearance of infection during the course of treatment. A + or a ++ reaction obtained only once, however, does not necessarily mean that gonorrhea is present; the reaction is not constant, and two or three tests are necessary for infallible results.

Journal de Chirurgie, Paris

36: 1-160 (July) 1930

*Methods of Restoring a Thumb. R. Gueullette.—p. 1.

Methods of Restoring a Thumb.—Gueullette gives the following classification of standard methods of restoring a thumb: (1) methods that utilize remaining parts of the mutilated hand, either phalangization of the first metacarpal or making the index finger a thumb; (2) methods of digital transplantation, using either a big toe or a finger of the other hand, and (3) methods of reconstruction that include successive cutaneous and osseous grafting (Nicoladini-Pierce method), simultaneous cutaneous and osseous grafting (Neuhauser-Albee method), and simultaneous cutaneous and osseous grafting after preliminary transplanting of the osseous tissue ((Schepelmann-Cotte method). The deciding factor in choosing the method to use is the social and economic status of the patient and the way the thumb will be used. For the hand of a workman a solid, strong thumb is important with no particular need for flexibility at the end, especially if the metacarpal is left. The Nicoladini-Pierce method seems best suited for this purpose. However, if the thumb is not to be used for labor and esthetic considerations enter into the decision, the most satisfactory results will be obtained by the grafting of a big toe. This will give a more natural looking and flexible thumb than the Nicoladini-Pierce method, although it will not be as solid.

Paris Médical

2: 157-168 (Aug. 23) 1930

Clinical and Therapeutic Classification of Rheumatic Pneumopathies. G. Caussade and A. Tardieu.—p. 157.
Actinotherapy of Wounds and Burns. P. Lemariée.—p. 161.
*Pathogenesis of Cardiac Accidents in Toxic Adenoma of Thyroid and in Exophthalmic Goiter. R. Froyez.—p. 164.

Cardiac Accidents in Toxic Adenoma of Thyroid.—Froyez says that experiments on animals, made by himself and others, show that disturbances in the thyroid secretion, especially its iodine content, affect the cardioregulatory system. However, the persistent arrhythmic conditions found in toxic adenoma of the thyroid and in exophthalmic goiter are due to some myocardial lesion.

Presse Médicale, Paris

38: 1137-1152 (Aug. 23) 1930

Urea Content of Blood and Ambard's Formula in Diabetes Mellitus. M. Labbé, R. Boulin and Justin-Besançon.—p. 1137.
*Infantile Asthma, Pruriginous Dermatoses and Hepatic Insufficiency: Infantile Arthritism Syndrome. H. Jumon.—p. 1138.
Causes of Onset of Labor. J. Fontes.—p. 1140.

Infantile Asthma, Pruriginous Dermatoses and Hepatic Insufficiency: Infantile Arthritism Syndrome.—Jumon says that asthma, certain pruriginous dermatoses and hepatic disturbances in young children form a homogeneous clinical ensemble. Although they never appear simultaneously, two or three often appear successively or even alternately in the same child and have the same pathogenesis, consisting of an alteration of nutrition, either hereditary or acquired, which predisposes the organism to factors otherwise harmless. This causes an instability of the body fluids and of the neurosympathetic system which reacts specifically in asthma, dermatoses or hepatic disturbance. These reactions are benign and tend to disappear before the age of 8 or 10 years. General methods of treatment which improve the alimentary system, and attention to diet and climatic conditions, produce the best curative results. The syndrome of this entire group of reactions may be termed the "infantile arthritism syndrome." In general, the successive appearance of two or more of these diseases in the same child is indicative of the source of the condition.

38: 1153-1168 (Aug. 27) 1930

*Ileus Reflex in Course of Renal and Ureteral Lithiasis. D. Denéchau and R. Prieur.—p. 1153.
Colorimetric Quantitative Determination of Nitrogen in Blood: Semimicromethod. A. Cassuto.—p. 1155.

Ileus Reflex in Course of Renal and Ureteral Lithiasis.—Denéchau and Prieur point out the importance of distinguish-

ing the ileus reflex in the development of renal and ureteral lithiasis from similar disturbances due to appendicitis, peritonitis and other sources. The principal symptoms to be observed are the sudden, violent beginning of the condition with intense pain in the abdomen (usually on the right), vomiting, intestinal retention and dysuric disturbances, and distention of the abdomen. The urine usually contains albumin, crystals of uric and oxalic acid and erythrocytes. The condition is caused by the penetration of a calculus into the ureter, which irritates the perirenal ureteral plexus and by the mesenteric nerves causes a reno-intestinal reflex, sometimes with spasmodic contraction. Relief is felt when gas and feces are expelled from the intestine, together with the calculus itself. The entire evolution of the disturbance rarely exceeds ten or twelve days. The secret of treatment is abstinence from operation, since intervention is always useless and often causes fatal results and the disease is sure to terminate in normal evacuation of the intestine in a few days. Palliative treatments to relieve pain and to stimulate normal intestinal action are recommended.

Revue Française de Gynécologie et d'Obst., Paris

25: 497-544 (Aug.) 1930

Internal Version in Cases of Cephalic Presentation with Pelvis Contracted at Inlet. J. Vanverts.—p. 497.
*Death of One Twin in Course of Gemellary Pregnancy. E. Aburel.—p. 510.

Death of One Twin in Course of Gemellary Pregnancy.—Aburel says that when some pathologic factor, as the presence of syphilitic or tuberculous infection, causes the death of one fetus, the reduced intensity and slow development of the infection often allows the other fetus to develop normally. The unequal resistance of the two twins is due to an accidental knot or loop in the cord or to malformation. When death takes place shortly before term, the diagnosis of gemellary pregnancy is obvious. When death occurs earlier, however, excessive nausea and vomiting, as well as the fact that the uterus is unusually large at first, seeming to indicate gemellary pregnancy, and then tends to resume normal developments, with diminution of the fetal movements, are important pathognomonic indications. After the rupture of the membranes the amniotic fluid is chocolate colored from the macerated dead fetus. Delivery is usually normal and a little before term. The living twin usually is born first. In case of cesarean section it is necessary to ascertain by touch which is the living twin (the dead fetus is softer). The results of confinement are usually good. The living twin rarely suffers from the infection that killed the other twin and is normal in development.

Revue Neurologique, Paris

2: 1-192 (July) 1930

Subacute Necrotic Myelitis: Anatomic and Clinical Considerations. L. van Bogaert, R. A. Ley and F. Brandes.—p. 1.
*Cerebral Tumors as Cause of Epilepsy. E. Moniz.—p. 18.
Opportunity for Suboccipital Drainage in Certain Endocranial Injuries. F. Ody.—p. 28.

Cerebral Tumors as Cause of Epilepsy.—Moniz says that cases of epilepsy that do not yield to ordinary methods of treatment, especially if they are of long duration and show jacksonian characteristics, are often due to cerebral tumors. Four cases are cited. In such cases roentgen examination reveals the presence of calcified tumors. If roentgen examination gives no results, arterial encephalography may be practiced to determine the presence (or absence) of tumors that do not produce opacity to roentgen rays.

Policlinico, Rome

37: 1129-1164 (Aug. 4) 1930. Practical Section

*Symptomatic and Spontaneous Meningeal Hemorrhages. V. Cavalletti.—p. 1129.
"Surgical Abdomen" Due to Impalement: Case. E. Capecchi.—p. 1133.
Introflexed Sutures. G. Baggio.—p. 1135.

Symptomatic and Spontaneous Meningeal Hemorrhages.—Cavalletti reports five cases of meningeal hemorrhages and makes certain observations on their symptomatology and pathogenesis. The treatment can be only symptomatic. The prognosis is favorable. Lumbar puncture aids in establishing the diagnosis and is, at the same time, the preferable form of treatment.

37: 309-360 (July 15) 1930. Surgical Section

*Primary Tumors of Liver. M. Ascoli.—p. 309.
*Hypernephroid Tumors of Kidney. G. Cicala.—p. 331.

Primary Tumors of Liver.—Ascoli analyzes the clinical histories of sixteen patients admitted to the Clinica chirurgica of Rome with a diagnosis of primary tumor of the liver. Two cases involved hepatic gummas; four, sarcomas; six, epitheliomas; one, a lymphangio-endothelioma; one, a cavernoma, and in two cases the diagnosis was only clinical. The malignant tumors have a rapid course, characterized by fever, pains, marked enlargement of the liver and ascites. The epitheliomas (chiefly hepatomas) occur in advanced age, while the sarcomas develop nearly always before the age of 40. In the cases of malignant tumors, one found in the history of the patients chronic inflammatory and degenerative lesions of the liver, sometimes also echinococcus cysts. The author discusses also the special diagnosis of gummas and hepatic abscesses.

Hypernephroid Tumors of Kidney.—Cicala points out that large benign tumors of the kidney present the greatest diagnostic difficulties and in most cases are diagnosed only at the operating table. In any case in which the diagnosis appears for various reasons doubtful, recourse should be had to exploratory laparotomy, the patient being prepared and everything being made ready for whatever operative act proves to be necessary. It should always be kept in mind that hypernephroid tumors are of long duration and occur almost always in adults, whereas sarcomas are more frequent in young persons, and mixed tumors more frequent in children. The prognosis in hypernephromas is exceedingly grave. Nephrectomy gives rarely good remote results. Recurrences are not infrequent. Only early interventions furnish hope of a radical recovery; yet early treatment is only rarely applicable. Patients often refuse to submit to an operation because of fear and because their symptoms undergo a temporary attenuation and they hope for a recovery without operation. Sometimes their medical advisers confine themselves to prescribing useless direct symptomatic remedies to combat the most alarming symptom—hematuria, which, as is well known, by reason of its periodic nature, reappears at long intervals, during which the patient enjoys perfect well being. All this causes a grave postponement of surgical intervention and makes the prognosis still more unfavorable. If a hypernephroma is diagnosed, nephrectomy should be done soon, for a good outcome, and especially the remote results, depend on an early operation. The contraindications result solely from the inevitable complications of cases tardily diagnosed (massive adhesions; paravertebral, axillary, inguinal or bone metastases). Cachectic or anemic appearance, varicocele or the large volume of the tumor does not, however, constitute a contraindication. The author prefers the extraperitoneal method of nephrectomy. He advises against routine removal of the suprarenals in all cases, as advocated by Grégoire—he recommends removal only when they are invaded by the tumor. The chief causes of death after the intervention are shock, hemorrhage, pulmonary embolism and reflex anuria. Recurrences develop (if at all) usually during the first year after the operation—either in the crater itself or in adjacent tissues. There may be metastases in distant organs, especially in cases coming late to operation.

Riforma Medica, Naples

46: 997-1032 (June 23) 1930

Vertebral Arthritis and Trauma. V. Putti.—p. 999.
Hypochloremia. C. Achard.—p. 1005.
*Medullary Lymphoblastic Leukemia. D. Liotta.—p. 1011.

Medullary Lymphoblastic Leukemia.—Liotta points out particularly that his case is significant because of the absence of active participation of the lymph nodes and of the spleen in a type of lymphoblastic leukemia and because the proliferating tissue remained localized exclusively in the myeloid organs, which justifies, according to Aubertin, the term "genuine medullary leukemia."

46: 1033-1068 (June 30) 1930

*Uricacidemia in Diabetes Mellitus. S. de Candia.—p. 1035.
Diaphragmatic Hernia. A. D'Istria.—p. 1037.
Algias and Their Treatment. F. Negro.—p. 1046.

Uricacidemia in Diabetes Mellitus.—De Candia states that hyperuricacidemia in diabetes mellitus signifies a distur-

bance of purine metabolism, although some authors, when it is not accompanied by true gouty symptoms, regard it as sometimes a simple functional and not always a pathologic alteration of the mechanism of the production and elimination of uric acid. Likewise, the low values of the uric acid in the blood circulation observed in some of his patients with grave diabetes must be interpreted as an alteration of purine metabolism, caused probably by a functional paralysis of the organ cells and by the retardation of the intra-organ oxidative processes, especially the liver. His results agree with those of Giorgi regarding the diminished elimination of uric acid in the urine in grave diabetes.

46: 1069-1108 (July 7) 1930

*Polypeptidorrhachia. N. Fiessinger.—p. 1071.
Organic and Functional Forms of Spasms and Tics. G. Colucci.—p. 1073.
Autochthonous Leprosy and Leprosy Contagion. A. de Amicis.—p. 1081.

Polypeptidorrhachia.—From his research, Fiessinger concludes, in harmony with Léon Michaux and Maurice Hérbain, that polypeptides may be found in the cerebrospinal fluid. These large molecules are of local origin or are from the blood. The passage of fluid between the blood and the spinal fluid does not occur in accordance with any constant laws of diffusion. Polypeptidorrhachia may accompany cerebral symptoms, bulbar symptoms or meningeal symptoms. These toxic syndromes are more accentuated, the greater the increase in polypeptides with respect to the total nonprotein nitrogen. The syndromes affect hepatic and renal insufficiency, which directly or indirectly produce the insufficiency of cleavage of the polypeptides. The influence of polypeptides on meningitis of toxic origin may henceforth be admitted. The meningeal reaction should not be considered the absolute and constant result of the polypeptidorrhachia, but in certain conditions it appears to the author as the dominant disturbance and the expression of the preponderant intoxication. The author regards his brief considerations on polypeptidorrhachia merely as a preliminary study.

Tumori, Milan

4: 301-402 (July-Aug.) 1930

Temperature of Neoplastic Tissues: Thermo-Electrical Measurements and Diagnostic Considerations. L. Barelli.—p. 301.
Provocation and Nature of Antineoplastic Forces. G. de Gaetani.—p. 344.
Lipomas of Spinal Meninges. I. Furiosi.—p. 350.
*Reaction in Vicinity of Neoplasms. A. Slaviero.—p. 359.

Reaction in Vicinity of Neoplasms.—Slaviero examined thirty-five malignant tumors for the purpose of studying possible inflammatory reactions in the involved area. After finding a constant inflammation and examining and interpreting the various elements, he thinks the manifestations are the expression, on the part of the organism, of an attempt to defend itself against the neoplasm.

Archivos Españoles de Pediatría, Madrid

14: 321-384 (June) 1930

*Toxicity of Viosterol. R. Garelly.—p. 321.
Treatment of Rickets with Viosterol: Roentgen Changes. J. L. Morales.—p. 336.
Climatotherapy in Bronchopulmonary Processes in Children. C. Sáinz de los Terreros.—p. 372.

Toxicity of Viosterol Used in Rickets in Infants.—Garelly has obtained good results with the administration of viosterol in the treatment of rickets. The degree of toxicity of viosterol, however, is not yet well determined and hence the advisibility of great care in the dose and administration of the drug. In cases in which it is necessary to administer the drug for a long time, the calcium and phosphate contents of the blood should be frequently determined as an index for the continuance or the stopping of the treatment. The author has never observed toxic phenomena caused by the administration of the drug. He has observed lack of appetite and dyspeptic disturbances as a result of the treatment. As soon as the disturbances appeared, the dose of the drug was temporarily diminished and then slowly increased, without the reappearance of the deleterious effects. The method that has given the author the best results is the following: The treatment is started with a dose smaller than that which is generally advised, and slowly increased (in accordance with the general condition of the infant and with the particular condition of his intestine), until reaching the proper dose (either prophylactic or curative dose).

Semana Médica, Buenos Aires

37: 77-152 (July 10) 1930. Partial Index

Fistula of Esophagus Following Mediastinal Pleurisy. M. Acuña and S. I. Bettinotti.—p. 96.
*Carbuncle in Diabetic Persons. R. Rodríquez Villegas.—p. 98.
Grave Hemorrhages as Complication of Gastric and Duodenal Ulcers. M. Cieza Rodríguez.—p. 101.
Syncytioma Malignum: Two Cases. E. L. Vila and G. F. Nunes.—p. 105.
Aplasia of Humerus and Exaggeration of Angle of Torsion: Case. O. F. Mazzini.—p. 108.
Hypertoxic Destructive Hydatidiform Mole: Case. A. I. Sosa y Sánchez and L. Rosenwasser.—p. 113.
Traumatic Spondylitis with Permanent Disability as Late Result of Accident. A. A. Masciotra.—p. 115.
*Exsiccated Alum for Permanent Dressings for Fractures, Dislocations and Diseases of the Joints. L. Benatuil.—p. 121.
Atropinized Charcoal in Treatment of Spastic Constipation and Other Diseases of Digestive Tract. Lefevre.—p. 133.

Carbuncle in Diabetic Persons.—Rodríquez Villegas says that carbuncles in diabetic persons should be removed early. Excision should include not only the necrotic area but also the area of subcutaneous cellulitis. Carbuncles in diabetic persons should be divided into two large groups thus: (1) benign or small lesions, similar to a union of furuncles, in which pain and edema are not intense and which as a rule develop in patients with benign diabetes, and (2) carbuncles of rapid development with intense pain and marked edema, which present a wide area of central necrosis and cause serious general disturbances, and which as a rule develop in patients with grave diabetes, who are generally obese and more than 50 years of age. In patients of the first group, treatment including cauterization with the actual cautery, passive hyperemia, phenolated fomentations, vaccinotherapy and roentgen rays may be sufficient. At the same time the progress of the diabetes should be determined frequently. If the patient does not improve under the treatment, excision should be resorted to. In grave cases of the second group, immediate and wide resection of the pathologic area, including the limits of the pyogenic infiltration of the cellular tissues, should be made. The author reports two cases: one of benign diabetes and acidosis due to the carbuncle and one of stationary diabetes reactivated by the development of the carbuncle. In both cases after an insufficient resection of the affected area a diffuse cellulitis dominated the clinical picture and necessitated a second intervention. Recovery ensued in both cases.

Exsiccated Alum for Dressings for Fractures and Diseases of Joints.—Benatuil prepared a mixture of 1,000 Gm. of exsiccated alum and 500 cc. of water to be used instead of plaster of paris, in making permanent dressing for fractures, dislocations and diseases of the joints. The substance transmits roentgen rays and solidifies twenty minutes after its application. After the dressing has been applied and before solidification of the mixture takes place, a roentgenogram may be made to determine whether the bones are in the proper position; if they are not, the dressing (which is still wet) may be removed and another attempt at reduction may be made.

Siglo Médico, Madrid

86: 29-56 (July 12) 1930

*Specificity of Streptococcus in Scarlet Fever, Erysipelas and Puerperal Fever. M. Salazar.—p. 29.
Anthropometry of School Children in Spain. D. E. Naval Galindo.—p. 30.
Psychiatric Legislation for Care of Persons with Psychoses. J. M. Sacristán, G. R. Lafora and J. Escalas Real.—p. 32.

Specificity of Streptococcus in Scarlet Fever, Erysipelas and Puerperal Fever.—Salazar says that the toxins of erysipelas and of puerperal fever cause a local skin reaction similar to that caused by the Dick test in scarlet fever. With the toxins of erysipelas or of puerperal fever, antitoxic serums, highly specific against the given infection, may be prepared. These serums cause the agglutination of the respective streptococcus. The discovery of the specificity of the toxins of scarlet fever, of erysipelas and of puerperal fever has resulted in a definite advance in the diagnosis and therapy of these serious

infections. By means of dermic reactions, susceptibility to the infections may be discovered and by the proper use of the suitable specific serums the diagnosis, the prophylaxis and the cure of these streptococcal infections may be obtained. The efficacy of specific serums is surprising and their superiority over polyvalent serums has been demonstrated. Each one of the three infections should be treated with the specific corresponding serum to obtain the exclusive action of the serum against its homologous toxin.

Deutsche medizinische Wochenschrift, Berlin

56: 1203-1246 (July 18) 1930

Criticism of Provocative Test for Gonorrhea. A. Stühmer.—p. 1203.
Shiga-Kruse Bacillus and Its Heterogenetic Antigen. B. Brahn and F. Schiff.—p. 1207.
Indications for Existence of Sympathetic Center for Blood Regulation. K. Moser.—p. 1209.
Relation Between Hypophysis and Hypertension. W. Hirsch.—p. 1211.
*Treatment of Meningitis During Epidemic in Shanghai. A. Virnich. —p. 1212.
Hyperthermy Treatment by Means of Paraffin in Rheumatic Diseases. H. J. Broichmann.—p. 1214.
Alleviation of Pain During Parturition. Frankenstein.—p. 1216.
*Treatment of Anemia in Children. H. Rau.—p. 1217.

Treatment of Meningitis During Epidemic in Shanghai.—During the meningitis epidemic in Shanghai, the intraspinal injection of polyvalent antimeningococcus serum brought favorable therapeutic results. In severe cases, lumbar puncture was at first done every day. Immediately after the puncture the serum was injected in a quantity somewhat smaller than the quantity of cerebrospinal fluid withdrawn. The serum injection never exceeded 25 cc. During the beginning stage this method of treatment was repeated every day. Later it was repeated after intervals of from two to three days, according to the severity of the case. In some patients the total amount of serum injected intraspinally reached 220 cc. On the days on which the spinal injections were omitted, the serum was injected intramuscularly. Virnich asserts that the administration of large quantities of serum did not lead to complications. He thinks that the low mortality rate was the result of the serum therapy. When the supplies of serum ran short, intravenous injections of methenamine were administered but this form of treatment was less effective than the serum therapy.

Treatment of Anemia in Children.—Rau states that among children the secondary anemias are more frequent than the primary forms. According to their etiology he classifies the forms of secondary anemia into alimentary, infectious, postinfectious, constitutional and helminthic. In discussing the therapy he stresses the value of a correct diet, administration of iron preparations, liver diet and blood transfusions. In many instances diet alone will counteract the anemia. Inorganic iron preparations are likewise effective in many instances. When liver therapy becomes necessary the liver should be given in the form of extracts, because in this form it is most easily taken by children. Blood transfusion is the most effective method, but even this is not helpful in all instances. In most cases it is difficult to decide which treatment will bring the best results. Accordingly, the author recommends that liver extracts and iron preparations be given simultaneously and in severe cases blood transfusion should also be employed. This combination therapy gives better results than if each method is employed alone.

56: 1291-1334 (Aug. 1) 1930

Peroral Immunization. H. Lubinski.—p. 1291.
Negative Results of Friedmann's Tuberculosis Vaccine in Treatment of Children with Tuberculosis. H. Fernbach.—p. 1295.
Ten Years' Experiences with Friedmann's Tuberculosis Remedy. Gettkant.—p. 1298.
Reflections on Fatal Results of Vaccination with Calmette's B C G in Lübeck. E. Friedberger.—p. 1300.
Principles of Infant Feeding. E. Stettner.—p. 1303. Concl.
*Treatment of Suppurative Meningitis. W. Mann.—p. 1306.
Serious Complications Caused by Intra-Uterine Pessaries. K. Tietze. —p. 1307.

Treatment of Suppurative Meningitis.—Mann points out that the prognosis in suppurative meningitis is still unfavorable. Numerous therapeutic methods have been employed; namely, lumbar puncture, administration of serum, protein therapy, serotherapy, and treatment with a solution of methenamine. The latter method, however, may cause complications in the central nervous system. Another treatment that has been employed successfully by several authors is the irrigation of the subarachnoid space following lumbar puncture, by means of physiologic solution of sodium chloride or Ringer's solution. Irrigations after suboccipital puncture have also been recommended. In some cases irrigations through the lumbar puncture might prove sufficient. However, in severe cases irrigations through the suboccipital puncture are necessary. The latter procedure permits a closer approach to the focus of suppuration, which is usually at the base of the brain, and it also prevents or counteracts adhesions. But because suboccipital puncture is more dangerous than lumbar puncture, it should be employed only if absolutely necessary. In most cases the irrigation has to be repeated every day or every second day. The author reports the results of irrigation treatment in three severe cases of suppurative meningitis. In all instances the cerebrospinal fluid became clear. In two instances the irrigation by means of lumbar puncture did not prove sufficient, and adhesions developed on the foramen magnum. In one of the cases the adhesions were overcome by irrigations through a suboccipital puncture. In the other case, in which suboccipital puncture had not been resorted to, the adhesion led to a fatal outcome. It was also found that the cerebrospinal fluid that was obtained by suboccipital puncture showed greater pathologic changes than the fluid that was obtained by lumbar puncture. Specimens of cerebrospinal fluid that had been obtained during the period of recovery always showed a spider-web coagulation from two to four hours after extraction. This proves that the sign is not pathognomonic for tuberculous meningitis.

Klinische Wochenschrift, Berlin

9: 1433-1480 (Aug. 2) 1930

Pathogenesis of Icterus Neonatorum. E. Volhard.—p. 1433.
Observations on Nutritional Allergy of Skin During Childhood. P. György, E. Moro and E. Witebsky.—p. 1435.
Preparation of Female Sex Hormone by Means of Precipitation. B. Zondek and C. van Eweyk.—p. 1436.
Operative Modification of Sugar Metabolism. F. Depisch, R. Hasenohrl and L. Schönbauer.—p. 1437.
Significance of Thyroid for Metabolism in Cold-Blooded Animals, Especially in Frogs. H. Henschel and M. Steuber.—p. 1442.
*Treatment of Anemia in Children by Means of Bone Marrow Preparation. W. Borchardt.—p. 1443.
*Attempt at Roentgen Treatment in Chronic Encephalitis. E. Trautmann and H. Pansdorf.—p. 1444.
*Serious Complications Following Treatment of Hernia by Means of Alcohol Injections. R. Goldhahn.—p. 1447.
Significance of Copper in Pathogenesis of Cirrhosis of Liver. R. Schönheimer and W. Herkel.—p. 1449.
*Lymphoid-Cell Sore Throat, Acute Lymphoidocytic Leukemia and Agranulocytosis. P. Lindemann.—p. 1451.

Treatment of Anemia in Children by Means of Bone Marrow Preparation.—On the basis of his experiences with red marrow from the ribs, which proved effective in experimental secondary anemia (*Deutsche med. Wchnschr.* **56**:521 [March 28] 1930; abstr. THE JOURNAL, June 14, 1930, p. 1962), Borchardt employed a bone marrow preparation, containing not only the hematopoietic factor but also the entire calcium of the bone, in the treatment of thirty-five anemic children, who were inmates of an orphan home. The hemoglobin content and the number of erythrocytes was low and some of the children were underdeveloped, had swellings of the cervical lymph nodes, had blepharitis and were pale. Their ages varied between 3 and 14 years. These anemic children were given a teaspoonful of the bone marrow preparation three times daily. The treatment was continued from December until March. The hemoglobin content, the number of erythrocytes and the body weight were determined weekly and a considerable improvement was noted. In several other inmates of the orphan home, who likewise were anemic and in poor health but who had not received the bone marrow preparation, improvement was hardly noticeable.

Attempt at Roentgen Treatment in Chronic Encephalitis.—Because irradiation with roentgen rays has been effective in many inflammatory processes, Trautmann and Pansdorf employed it in six cases of chronic encephalitis. The rays were applied on three fields, two temporal and one occipital. The distance was 40 cm. and the quantity was 10 per cent of a unit skin dose. A 0.5 mm. copper filter was used. The intervals between the irradiations were usually four days. The authors give the case histories of the six patients who were treated in this manner. In none of the cases was improvement noted.

Accordingly the authors conclude that in cases of chronic encephalitis roentgen treatment is not effective. This indicates that inflammatory processes in the brain differ from inflammations in other organs. The authors assume that the efficacy of roentgen rays in inflammations outside the central nervous system are due to their mobilizing effect on the function of the supporting tissue; their inefficacy in inflammations of the brain is due to the fact that the glia cells do not react to the roentgen rays like other supporting tissues.

Complications Following Treatment of Hernia with Alcohol Injections.—Goldhahn describes three cases of hernia in which alcohol injections caused serious complications, such as sepsis, fecal fistulas and injury of the vas deferens. Other authors observed ileus and gangrene of the testes following alcohol injections. Occasionally it might be possible to close a small hernial opening by the injection treatment. However, the results are doubtful and, in view of the serious complications that might result, alcohol injections should no longer be employed for treatment of hernia. Because some physicians still employ this "nonsurgical" method, the author considers it necessary that the medical press should warn against it.

Relation Between Diseases of Blood and Diseases of Mucous Membrane of Mouth.—Lindemann directs attention to the correlation between diseases of the blood and diseases of the mucous membrane of the mouth. He mentions the soreness of the tongue in pernicious anemia. Then he reports the clinical histories of three patients who showed such symptoms as sore throat, soreness of the tongue and soreness of the gums. Careful examination of the blood revealed abnormal conditions. In the conclusion the author stresses that a blood count is advisable whenever inflammations in the pharyngeal region show some unusual aspects.

Biochemische Zeitschrift

9: 1481-1528 (Aug. 9) 1930

Specific Effects of Pharmaceutic Preparations Necessary to Influence Pathologic Reaction of Organism. H. Langecker.—p. 1481.
Interference in Vasomotor Regulation. H. Rein.—p. 1485.
*Modification of Basal Metabolism by Thymus and Spleen Extracts. M. Schneider and A. Nitschke.—p. 1489.
Action of Hormonal Preparation from Anterior Lobe of Hypophysis on Male Genitalia. E. J. Kraus.—p. 1493.
*Pulmonary Foci in Lymphogranulomatosis. E. Saupe.—p. 1495.
Method for Testing Function of Stomach. L. Dinkin and Z. Lichtig. —p. 1499.
Criticism of Microdetermination of Nitrogen-Containing Substances in Urine. D. Jacoby.—p. 1501.
Experiments Contradicting Guanidine Theory of Tetany. G. Berencsy and K. Zinhobel.—p. 1503.
Tests for Demonstration of Cancer Lysin in Blood Serum of Patients with Cancer. H. Lehmann-Facius.—p. 1504.

Modification of Basal Metabolism by Thymus and Spleen Extracts.—In the first part of the article, Schneider and Nitschke review the observations of various authors on splenectomized and on thymectomized animals. They further report that Nitschke succeeded in extracting from the thymus two substances, of which the one effected a decrease in the calcium content of the blood of rabbits and the other reduced the inorganic phosphorus content. The substances were detected also in the spleen and in the lymph nodes; that is, in the entire lymphopoietic system. In other organs, however, they could not be found. In order to determine whether extracts from the spleen and thymus influence the basal metabolism, the authors made tests on guinea-pigs. Experiments with the substance that reduces the calcium content of the blood proved that it has no influence on the basal metabolism. However, the extract that reduces the phosphorus content, and which is extracted from the spleen and thymus by means of acetic acid-alcohol and ether, decreased the basal metabolism not only in normal animals but also in those in which the basal metabolism had been increased by means of thyroxine. The average reduction was 22.9 per cent. The thymus and spleen extracts used for the experiments contained neither proteins nor fats. The injections were given subcutaneously. Control experiments were made with liver and muscle extracts, hypertonic solutions of sodium chloride and other extracts. However, an influence on the basal metabolism was not observed.

Pulmonary Foci in Lymphogranulomatosis.—Saupe maintains that the pulmonary foci in lymphogranulomatosis are not as rare as is assumed by many authors. As proof he cites his observations on ten patients and reports by other authors. However, he admits, and by that confirms the statements of other authorities, that pulmonary foci of lymphogranulomatosis are only rarely diagnosed roentgenologically because other pathologic processes show similar roentgenograms. Cancer of the hilus of the lung with large mediastinal metastases gives almost the same roentgenogram as pulmonary lymphogranulomatosis. However, the bilateral broadening of the mediastinum speaks more for lymphogranulomatosis, the unilateral broadening more for cancer of the hilus. Lymphogranulomatosis of the lung is often accompanied by pleuritic exudates or transudates and by bronchopneumonic processes, and these conditions mask the lymphogranulomatosis and it is not recognized in the roentgenogram. The author also discusses the relation between pulmonary tuberculosis and lymphogranulomatosis. In one case reported by him there existed a disseminated pulmonary tuberculosis and the mediastinal lymph nodes were affected with lymphogranulomatosis. However, there were no granulomas in the lungs. Regarding the therapy of lymphogranulomatosis, the author states that roentgen irradiation often brings improvement. However, it is usually only temporary. Postmortem examinations proved the frequency of bone involvement in lymphogranulomatosis.

Medizinische Klinik, Berlin

26: 1139-1174 (Aug. 1) 1930

Occlusion of Coronary Arteries. W. Koch.—p. 1139.
Treatment of Acute Nontuberculous Pleural Empyema. F. Smoler.—p. 1142.
*Irradiation of Body Cavities by Means of Ultraviolet Rays Produced Therein. S. Westmann.—p. 1146.
*Pathogenesis and Therapy of Tuberculous Hemoptysis. H. Edel.—p. 1148.
Panagglutination in Agranulocytic Reaction. W. Hochheim and G. Rosenthal.—p. 1150.
Treatment in Weakness of Uterine Contractions and During Placental Stage. H. Krukenberg.—p. 1150.
Ehrlich's Diazo Reaction After Roentgen Irradiation in Lymphogranuloma. K. Tschilow.—p. 1151.
Malformation of Kidneys. R. Rittmann.—p. 1153. C'cn.
Blood Groups Among Patients with Leprosy in Latvia. M. Weidemann. —p. 1155.

Irradiation of Body Cavities by Means of Ultraviolet Rays Produced Therein.—Westmann points out that attempts have been made to irradiate the body cavities with ultraviolet rays. In order to introduce the rays, quartz mirrors were used; but, as this method proved unsuccessful, an instrument was perfected that would produce the ultraviolet rays within the body cavity. The apparatus consists of a bipolar spark-gap that is enclosed in a quartz tube. Quartz is likewise used for insulation of the conducting wires. The author gives illustrations and a detailed description of the instrument. The efficacy of the instrument was tested on animals. In the conclusion the author mentions conditions in which the instrument might prove of therapeutic value.

Pathogenesis and Therapy of Tuberculous Hemoptysis.—Edel discusses two forms of hemoptysis. To the first group belong the minor hemorrhages that usually continue for longer times and in which the blood does not escape from ruptured vessels but rather by diapedesis. To the second group belong the fulminant hemoptyses, which result from the rupture of aneurysmal pulmonary vessels. The first group may be due to various factors, to an increased permeability of the capillary walls, to toxic injuries, to sympathetic or incretory disorders, to inflammatory hyperemia and to meteorological conditions. In the diapedesis hemorrhages there generally exist serious pneumonic or productive, nonshrinking processes. The profuse fulminant hemorrhages usually occur when large parts of the lung contract as the result of chronic processes. The vessels become constricted by compact connective tissue indurations. Emphysematous conditions in the other parts of the lung and cardiac decompensation promote the stasis in the stenosed vessels. Then varicosis develops and the thin, dilated wall of the vessel ruptures from the slightest irritation, such as an attack of coughing. Between these two main forms stand the hemorrhages from the scars at the apex of the lung and the initial hemoptysis in early infiltrates. Both of these are arrosion hemorrhages and are of minor intensity. The fact that the same pathologic conditions in some persons lead to hemoptysis and in others do not, shows that certain constitutional factors must be involved, as diathesis, toxic injury of the walls of the vessels

and coagulation anomalies. In discussing the therapy of hemoptysis the author states that the first aim should be to increase the coagulability of the blood. He points out that the mechanism of coagulation is as yet not entirely understood. Some consider it a chemicosynthetic process and others a colloidochemical process. The pharmacodynamic mechanism of most hemostatics is not clear and, according to the author's experiences, most of them fail in severe hemorrhages because they supply only one factor involved in the process of coagulation. The author further mentions several hemostatics and shows their shortcomings. Then he discusses the methods that he has found helpful. Minor hemorrhages, even if they continue for some time, do not endanger the life of the patient and do not necessitate therapeutic intervention. The patient should be kept quiet, coughing should be counteracted, and care should be taken that the patient has regular bowel movements. A thorough clinical examination should not be made until two days after the bleeding has ceased. The author asserts that the use of hemostatics never caused an earlier cessation of the hemorrhage than in cases in which a hemostatic was not used. On the contrary, he noted an increase in the hemorrhage following intravenous injection of calcium preparations. Profuse hemoptysis, which endangers the life of the patient, requires prompt therapeutic action. Most hemostatics, with the exception of protein injections, were failures in these conditions. Collapse of the bleeding lung by means of pneumothorax is advisable only if it is known which side of the lung is affected. As the best method the author recommends blood transfusion. He employed it successfully in eighteen cases of tuberculous hemoptysis. The usual amount transfused was from 80 to 100 cc.

Münchener medizinische Wochenschrift, Munich

77: 1221-1260 (July 18) 1930. Partial Index

Syphilis of Auditory Organ. A. Güttich.—p. 1221.
Action of Hormones in Gynecology. P. Hauptstein.—p. 1223.
*Treatment in Collapse Caused by Arsphenamine Injection. F. Wirz.—p. 1225.
*Increase in Cancer in Bavaria. V. E. Mertens.—p. 1227.
Method for Photography in Medicine and in Other Sciences. W. Comberg.—p. 1234.
Functional Tests of Heart by Means of Blood Pressure Curves After Exertion. E. Baráth.—p. 1235.
Methods in Psychotherapy. J. H. Schultz.—p. 1237.

Treatment in Collapse Caused by Arsphenamine Injection.—Wirz states that the collapse conditions that sometimes develop after injection of arsphenamine occasionally have a fatal outcome. He describes the clinical aspects of arsphenamine collapse and then discusses its pathogenesis. Postmortem examination of a patient who had died in an arsphenamine collapse proved that the heart and the peripheral vessels were almost empty. The arteries are strongly contracted during the collapse and the administration of circulatory stimulants is frequently ineffective. Therefore the author recommends that the vascular tonus be improved by the application of heat. He gives two case reports in which he employed this method. The patient was placed immediately in a hot bath. Already after half a minute the sallow, greenish-blue skin became reddish, the pulsation was again perceptible and consciousness returned. The patient remained in the bath for five minutes. Then he was wrapped in blankets and camphor was administered. After several hours he had recovered sufficiently so that he was permitted to go home. Similar favorable results with the hot bath were obtained in a woman who had suffered an arsphenamine collapse. In the conclusion the author points out that the hot bath might also prove helpful in other forms of collapse.

Increase in Cancer in Bavaria.—Mertens discusses various shortcomings in medical statistics and especially in statistics regarding cancer. Official reports indicate that cancer is on the increase in Bavaria. The author points out that many authorities believe that this increase is only apparent and not real. Two factors are usually cited as being responsible for the apparent increase, namely, the fact that modern diagnostic methods detect a larger number of cancer cases and also that a larger number of persons reach the higher age groups, and cancer is mainly a disease of the aged. However, careful analysis of the statistics convinced the author that these statements are not entirely correct and that there is a real increase in the number of fatalities from cancer.

77: 1311-1352 (Aug. 1) 1930. Partial Index

Determination of Circulatory Minute Volume in Human Beings by Fick's Method of Obtaining Mixed Venous Blood by Means of Catheterization of Heart. O. Klein.—p. 1311.
*Influence of Muscle Extract on Heart. I. Bagdassarjanz and M. Turkeltaub.—p. 1314.
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Results of Examinations with Simplified Serologic Method of Müller's Conglobation Reaction. B. H. U. Mohrmann and B. Hajos.—p. 1317.
Vesicle Formation on Hands of Dishwashers Caused by High Temperature of Water. F. Lanyar.—p. 1320.
Possibility of Detoxicating Intestinal Contents by Means of Spring Water That Contains Sodium Sulphate and Magnesium Sulphate. O. Neustätter.—p. 1320.
Gas Permeability of Living Skin in Gas Baths and in Carbon Dioxide Water Baths. S. Hediger, Zürich and Tarasp.—p. 1321.
Effect of Decline of Mortality on Life Insurance. P. Hörnig.—p. 1323.

Influence of Muscle Extract on Heart.—Bagdassarjanz and Turkeltaub direct attention to Schwarzmann's investigations on the efficacy of muscle extract in the treatment of angina pectoris. They name several other authors who successfully employed the extract (from striated muscles of calves) in various cardiac disorders. The authors themselves gave subcutaneous injections of the muscle extract in fifty-four cases, and they tested the efficacy of the treatment by means of the electrocardiograph. They give the case histories of nine patients. Their observations are summed up as follows: 1. Under the influence of the extract the frequency as well as the intensity of the pains become reduced. 2. In patients with hypertension the blood pressure decreases, in those with hypotension it increases, and in normal persons the pressure either decreases slightly or remains unchanged. 3. Following the injection the cardiac rhythm becomes slower. 4. This retardation can be demonstrated with the electrocardiograph in the tenth minute after injection. 5. The retardation of the rhythm lasts longest in patients with tachycardia. In patients with bradycardia the rhythm becomes somewhat accelerated from forty to sixty minutes later.

Wiener klinische Wochenschrift, Vienna

43: 961-992 (July 31) 1930

Results of Primary Operative Treatment of Wounds. F. Felsenreich.—p. 961.
Clinical Aspects and Therapy of Rupture of Kidney. R. Friedrich.—p. 964. C'td.
Treatment of Severe Bilateral Contracture of Hips. G. Haberler.—p. 967.
Indications for Transperitoneal Nephrectomy. K. Haslinger.—p. 970.
*Adenoma of Mammary Gland During Pregnancy. W. Kreibig.—p. 972.
*Resection of Duodenal Ulcer. F. Mandl.—p. 974.
Roentgenoscopy of Normal Urinary Organs by Means of Intravenous Injection of Contrast Medium. J. Palugyay.—p. 978. C'td.
*Surgical Diathermy in Treatment of Wounds. W. Spitzmüller.—p. 981.
Late Results of Closed Injuries of Brain and Their Influence on Duration of Life. H. Steindl.—p. 985.
Restorative Surgery of Biliary Tract: Case of Hepatocholangioduodenostomy. F. Stöhr.—p. 990.
Animal Experiments on Syphilis of Kidney. M. Friedmann.—p. 992.

Adenoma of Mammary Gland During Pregnancy.—A woman, aged 18, in the fourth month of her first pregnancy, had always been healthy. Three weeks previously, however, she had noticed a small nodule in her right breast, which grew rapidly. Examination revealed a firm nodule in the upper external quadrant of the right breast. It was diagnosed as a fibroadenoma. The tumor was extirpated. It showed no connection with the parenchyma of the gland. Microscopic examination revealed that it was an encapsulated epithelial formation in which connective tissue occurred only in the form of small septums that divided the lobes. The lobes showed the structure of a mammary gland. In reviewing the literature, Kreibig found reports of two similar cases. Both of the patients were young, aged 20 and 21, respectively, and in both the growth became noticeable during pregnancy. The author comes to the conclusion that these adenomas have a certain relation to pregnancy and that they might be considered as adenomas that hypertrophied as a result of pregnancy. These adenomas are the tubular form. They are noteworthy not only because they are comparatively rare but also because they show to what extent an abnormal growth may adapt itself to the surrounding tissues, and they also prove that a tumor of the breast with rapid development during pregnancy is not necessarily a malignant growth.

Resection of Duodenal Ulcer.—In the first part of the article, Mandl mentions the various surgical methods that are

employed for the treatment of peptic ulcers. In the second part he gives a statistical report on cases of duodenal ulcer. Cases in which gastro-enterostomy was done are not discussed, but the author reports eighty-one cases in which resection was performed. In thirty instances Finsterer's modification of the Billroth II operation was employed, and in fifty-one cases his resection for exclusion was done. In the latter method, unilateral exclusion of the pylorus is combined with an extensive resection of the stomach. The aim of the method is sure exclusion of the ulcer and a healing of it, and the object of the extensive resection of the stomach is to do away with hyperacidity and thus prevent an ulcer in the jejunum. Of the thirty patients in whom resection was done twenty were entirely free from pain, six were improved, two died and two were not improved. Of the fifty-one patients in whom resection for exclusion was done thirty-four were cured, eight showed improvement, two died, and seven were not improved. The statistical report is followed by a critical evaluation of surgical methods that are employed in the treatment of peptic ulcers. In the conclusion the author states that, if definite signs of an ulcer are absent, surgical intervention is not indicated. Whenever an ulcer exists, resection is probably the best method because, if the ulcer is removed, hemorrhage and perforation are prevented. However, resection cannot always prevent a jejunal ulcer. Considering the physiology and the chemism of the stomach, it seems advisable that in all resections of an ulcer, the antrum and the pylorus should also be resected. Although the resection for exclusion improves the chances for a healing of the ulcer, it does not guarantee the cure. The operation does not prevent later hemorrhages or a jejunal ulcer. It is inferior to resection and whether it is better than gastro-enterostomy cannot be decided as yet.

Surgical Diathermy in Treatment of Wounds.—Spitzmüller describes a method for the treatment of primary accidental wounds. It is a disinfection by means of surgical diathermy. The author reports his observations in 100 cases. He asserts that infection was prevented in all instances. He therefore recommends that disinfection by means of surgical diathermy be tried in other cases, and he thinks that it will prove to be superior to disinfection by excision with the surgical knife.

Zentralblatt für Chirurgie, Leipzig

57: 1969-2032 (Aug. 9) 1930

*Continuous Evacuation of Stomach by Way of Nares in Treatment of Postoperative Ileus. C. E. Jancke.—p. 1971.
*Treatment of Actinomycosis with Lymph Node Preparations. F. Trauner.—p. 1974.
*Operation for Ectopic Urinary Bladder. F. Roloff.—p. 1977.
*Plastic Operation for Repair of Diastasis of Abdominal Rectus Muscles. A. Abrashanow.—p. 1979.
Blood Supply of Tongue. D. Wasa.—p. 1981.
Use of Pedicled Skin Flaps to Cover Skin Defects. K. Tiesenhausen.—p. 1985.
New Instrument for Endovesical Electrocoagulation. E. Bors.—p. 1988.

Continuous Evacuation of Stomach in Treatment of Postoperative Ileus.—Jancke feels that this procedure has not received the recognition it deserves. Passing the tube through the nares has distinct advantages over swallowing the tube. A favorable effect is noted within a few hours. If not, the tube may be left in place for twelve hours at a time, when it should be removed to obviate the occurrence of ulcers in the esophagus. If after forty-eight or sixty hours the ileus has not disappeared, enterostomy is indicated. He has never performed a gastrostomy. The tube meets every expectation that a gastrostomy would and is much better for the patient. Five cases are cited.

Treatment of Actinomycosis with Lymph Node Preparations.—Having noted that actinomycosis develops only in tissues free from lymph nodes, Trauner concluded that it probably would be advantageous to add to the usual treatment of this condition an injection of lymph node juice, or an extract, alcoholic or aqueous. He used mostly the cervical lymph nodes of cattle but also took some from horses. The amount was 1 or 2 Gm. of gland substance in 1 cc. of fluid. This was embodied in the dressings, instilled into the abscesses or fistulous tracts and finally was injected into the cicatricial tissue. The effect of this treatment was apparent after a few days.

Operation for Ectopic Bladder.—Roloff reports two cases in which he performed Maydl's operation for this condition. One patient was a woman who had been operated on eighteen years previously. She married recently and became pregnant. Because of an increasing tetany of the uterus which could not be controlled medically, a cesarean section was performed. Both mother and baby died. The cause of death was not determined. The point is that the patient had been well for eighteen years and that she went through the pregnancy without any disturbance that could be charged to the operation. The second patient was a boy, aged 15, operated on five years ago. He was in splendid condition at the time of reporting.

Plastic Operation for Repair of Diastasis of the Abdominal Rectus.—Abrashanow uses strips of fascia lata which are passed completely around the muscles, but only in cases in which the separation is greater than 10 cm. The anterior sheath of the muscle is then closed in the usual manner. This preserves the state of the muscle both anatomically and functionally.

Zentralblatt für Gynäkologie, Leipzig

54: 1857-1920 (July 26) 1930

Place of Production of Hormone of Anterior Lobe of Hypophysis During Gravidity. E. Philipp.—p. 1858.
Induction of Abortion by Means of Roentgen Rays. K. Bollag.—p. 1867.
*Advisability of Interruption of Pregnancy in Congenital Hereditary Cataract or in Tumor of Brain. C. Fleischmann.—p. 1870.
*Rupture of Aorta During Puerperium. S. Böhm.—p. 1874.
*Contraindicated Ecbolics. E. Puppel.—p. 1878.
Menstrual Cycle of Human Vagina. K. Dierks.—p. 1882.

Interruption of Pregnancy in Congenital Hereditary Cataract or in Tumor of Brain.—Fleischmann reports the case of a woman with congenital cataract of both eyes who was in the fifth month of pregnancy. The anamnesis revealed that cataract and amblyopia were hereditary in this family. In four generations, fifteen of thirty-four members had had these disturbances. From the eugenic point of view it seemed advisable, therefore, to perform an abortion. However, because an abortion in the fifth month is not without danger for the mother, it was decided that this time the pregnancy should be allowed to go to term. The woman gave birth to a healthy girl but five months after parturition she consented to be sterilized. The author regrets that in the present day laws regarding abortion eugenics are not taken into consideration. In the second part of the article he discusses the case of a gravida with a tumor of the brain. The pregnancy was not interrupted and the woman gave birth to a macerated male fetus. The mother died several weeks later. The author states that the concurrence of tumor of the brain and pregnancy is rare but he thinks that, if such a case occurs, a committee of medical authorities should decide whether an abortion is advisable.

Rupture of Aorta During Puerperium.—Böhm reports a case in which rupture of the aorta caused the death of a woman, aged 31, on the sixth day after parturition. Examination before the beginning of labor revealed that the heart was enlarged in both directions, especially on the left side. An abnormal systolic sound could be heard and the second aortic sound was accentuated. The birth was spontaneous. On account of the cardiac disorder, the heart action of the mother was carefully observed, but complications did not develop. The postpartum period was normal up to the fifth day, when the patient felt a sudden sensation of pressure behind the sternum. She died eighteen hours later. At first it was thought that death was caused by thrombosis, by embolism or by heart failure, but the necropsy revealed a rupture of the aorta. The author further discusses the various conditions that may lead to rupture of the aorta. He mentions congenital weakness of the aorta, syphilis, pregnancy and the puerperium. One of these factors or several combined and an abnormally high blood pressure led to the rupture of the aorta. The case shows that, if an insufficiency of the aorta is detected during the early stage of pregnancy, interruption of pregnancy might be advisable.

Contraindicated Ecbolics.—Puppel is of the opinion that the potent ecbolics are employed more often than is advisable and that they may lead to rupture of the uterus. He discusses several ecbolics and states when they should be used and when they are not advisable. Ecbolics are indicated in cases of

abortion especially when the patient is feverish. During parturition, ecbolics are indicated only during the period of expulsion when the head is on the floor of the pelvis and is nearly visible. At this point the gravida often loses her strength. During the placental stage the intravenous administration of an ecbolic is advisable if hemorrhages set in and when the expulsion of the placenta is retarded. In a cesarean operation an ecbolic should be administered after the extraction of the child. However, in cases of primary weakness of the labor pains during the period of dilatation, ecbolics are contraindicated. Their use is also not advisable when during the period of expulsion the labor pains become weak as a result of exhaustion. Ecbolics are likewise contraindicated when the uterine contractions are strong enough but extremely painful, for in these instances there exists a danger of rupture of the uterus. In all instances in which the physician thinks an injection necessary, he should observe the patient for some time before he gives it. Midwives should not be permitted to give injections.

54: 1921-1984 (Aug. 2) 1930

Results of Quantitative Determination of Sex Hormone. P. Schuschania.—p. 1924.
Causes of Onset of Labor. M. L. Perez.—p. 1937.
Congenital Gaps in Skull as Causes of Intra-Uterine Death of Fetus. H. Baumm.—p. 1938.
Comparative Statistics on Legalized and Nonlegalized Abortions. M. Magid.—p. 1939.
*Care of Umbilical Stump. M. Karp.—p. 1947.
Congenital Generalized Dropsy in the New-Born. F. Kovács.—p. 1948.
Davis' Cancer Reaction. S. Jagunow.—p. 1954.

Care of Umbilical Stump.—Karp points out that the opinions of authorities differ as to whether it is more advantageous to sever the umbilical cord close to the skin margin of the umbilicus or farther away. Some advise a close division to make the asepsis less difficult, and this method is practiced in the majority of obstetric clinics. However, the disadvantage of the procedure lies in the fact that, if an infection develops, the way to the peritoneum is short and the danger of peritonitis is greater. The difficulties of a possible secondary hemorrhage in case of a close division should likewise not be underestimated. To eliminate such difficulties the author adopted Scherbak's method. The umbilical cord is severed from 12 to 15 cm. away from the umbilicus. Following ligation of the stump about 2 cm. from the margin of the umbilicus the bandage is applied. Differing from Scherbak, the author applies to the umbilical stump a gauze compress, saturated with alcohol. He advises against ointment bandages. He has employed this method since 1925. Among 2,000 confinements, a subsequent cauterization of the umbilical stump was necessary in only six instances. In these cases a Paquelin cautery was employed.

Nederlandsch Maandschrift voor Geneeskunde, Leyden

17: 69-121, 1930

The Colitoxin. B. P. B. Plantenga.—p. 69.
Importance of Inorganic Metabolism in Pathology of Children. E. Gorter.—p. 84.
*Anemia with Icterus. F. J. Peljak.—p. 105.
Experimental Researches on Etiology of Scarlet Fever, Dairen, 1929. H. D. Boer.—p. 111.

Anemia with Icterus: Case in Child.—Peljak describes the peculiar case of a girl, aged 10. Up to the age of 5½, the patient was a healthy child and had a good color. She suddenly became ill with pain in the abdomen, squeamishness and high fever. She awoke the next morning with a yellow color of the skin, over her whole body. The urine was dark brown, and the stool had an unusual appearance. After ten days, the yellow tint had disappeared and the child was well again. At the same time a brother, one and one-half years older, presented precisely the same symptoms. He also had been well up to this time and had always had a good color. The mother doesn't remember whether either child was yellow the first few days after birth. The three following years after this morbid process, the girl again became yellow in the same month (August) as before. At the same time, she was languid and had no appetite. When 6½ years of age the child had a mild exanthematic disorder, at which time she was yellow, and had sore throat. At 10 she was still more or less yellow and was languid and apathetic; also the brother became paler and had several attacks of yellowishness of the skin, but, except for the slight icterus (especially of the sclerae), he was not ill. No other member of the family had ever had icterus. In the feces of the girl, a few oxyurids were found. Oil of chenopodium was administered and a large quantity of oxyurids were eliminated, as a result. The erythrocyte count was 3,030,000, and the leukocyte count was 10,000. Conspicuous in the blood was the large number of small chromocytes, which were dark red. These contrasted strangely with the usually larger and pale type. Hemolysis began in a 0.62 per cent solution of sodium chloride. In a 0.4 per cent solution about half of the erythrocytes were dissolved, and in a 0.3 per cent solution nearly all were dissolved. Normally dissolution begins with from 0.38 to 0.42 per cent solution, and total dissolution occurs with a 0.3 per cent solution. The child was given a diet with large quantities of milk, poor in fats but rich in raw fruit and green vegetables. To improve her appetite, she was given, three times a week, an ounce of liver, also syrup of ferrous iodide. Several days' rest in bed, at the start, was prescribed. She was left in the care of the family physician. When the author saw her five weeks later, the fatigued appearance had disappeared. She looked much better and had slightly pink cheeks, was not so yellow and had a good appetite. The blood picture, however, did not show much improvement. Roentgen irradiation of the spleen was tried for four weeks (five ⅔0 erythema doses). The spleen was possibly slightly reduced in size but the irradiation had no influence on the blood picture. The author thinks that, in spite of the improved condition of the child, only extirpation of the spleen will effect a permanent improvement in this case of hemolytic icterus. He is not prepared to say whether it is a question of congenital familial hemolytic icterus or whether the same noxa produced similar conditions in brother and sister, at the same time.

Norsk Magasin for Lægevidenskapen, Oslo

91: 833-912 (Aug.) 1930

*Recurrent Vomiting and Acetonemia in Children. L. Salomonsen.—p. 833.
*Unusual Complication in Regular Enucleation. H. G. A. Gjessing.—p. 844.
*Acute Intoxication Due to External Use of Resorcinol. A. Klem.—p. 849.
*Tuberculosis Among Medical Students. J. Heimbeck, O. Scheel, T. Skaar and O. Thorrud.—p. 851.
Diet Treatment in Tuberculosis. F. G. Dahll.—p. 854.
*Subphrenic Abscesses. B. Dahl.—p. 860.
Biologic Significance and Therapeutic Application of Magnesium. B. Dahl.—p. 877.

Recurrent Vomiting and Acetonemia in Children.—Salomonsen says that this disturbance is due to an exhaustion of the nervous system or certain parts of it, and treatment should be along psychic lines.

Unusual Complication in Regular Enucleation.—In Gjessing's case of advanced glaucoma, with excellent results after antiglaucomatous iridencleises with meridional iridotomy according to Holth in the better, right eye six years earlier, enucleation of the left eye under local anesthesia according to Seidel was followed by temporary complete amaurosis and continued defect in the field of vision. As the anterior chamber was half filled with blood and profuse hemorrhage was feared, twice the usual amount of solution of epinephrine hydrochloride was added to the anesthetic, i. e., 2 drops per cubic centimeter, or 10 drops, half of the maximal dose for subcutaneous application (Poulsson). The injury is believed due to the effect of the epinephrine on the already weakened eye.

Acute Intoxication Due to External Use of Resorcinol.—Klem's case shows that even 20 Gm. of 50 per cent resorcinol paste, applied to an intact skin, may be dangerous.

Tuberculosis Among Medical Students.—Heimbeck et al. state that, among 183 medical students with known cutireaction prior to their hospital service, seven cases of tuberculosis were established during the hospital term, one among the eighty-eight with positive cutireaction, six among the fifty-one with negative reaction, and none among the forty-four with negative reaction, vaccinated with B C G.

Subphrenic Abscesses: Diagnosis and Treatment.—On the basis of his thirty-two cases, Dahl discusses the clinical development of subphrenic abscesses and their anatomic orientation, different types, diagnostic adjuvants and treatment.